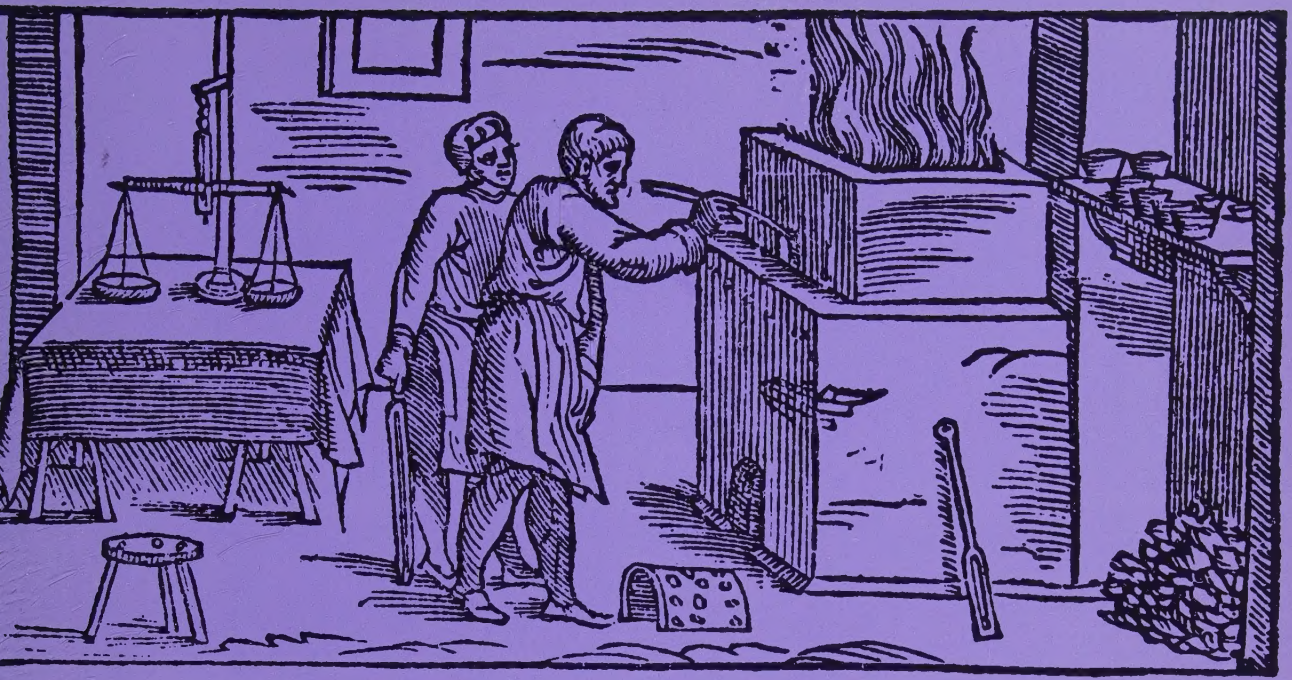

Science Museum

THE TECHNIQUES OF ANALYTICAL CHEMISTRY

H.M.N.H. Irving

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A Science Museum Survey

The Techniques of Analytical Chemistry
a short historical survey

by **H.M.N.H. Irving**

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Foreword

This short introduction to a subject of great social and scientific importance has been prepared in connection with the celebration of the centenary of the foundation of the Society of Public Analysts, which has developed into the present day Society for Analytical Chemistry. The Society has itself prepared a history of its foundation development and membership. The Science Museum's role in the celebration has been to mount a special exhibition under the title "You and your analytical chemist" in which emphasis was placed on the significance of analytical chemistry in everyday life. A full social history of analytical chemistry would be a substantial undertaking. Although the Science Museum might well one day attempt this, it seemed that the most appropriate publication it could produce on this occasion would be one of the studies of experimental techniques being undertaken by the Department of Chemistry under the supervision of Dr Frank Greenaway based on, but not confined to, objects in the chemistry collections.

It has been written at the joint invitation of the Science Museum and the Centenary Organising Committee of the Society for Analytical Chemistry by Professor H.M.N.H. Irving of Leeds University, distinguished for his contributions to the theoretical background of analytical chemistry.

The Museum is grateful to the Society and to Professor Irving for their joint contribution to the growing body of Science Museum studies in the history of science.

Margaret Weston
Director

Introduction

A previous Science Museum book *The Chemical Balance,* described the instrument which made chemistry into an exact science with a self-consistent quantitative theory. This booklet, by Professor H.M.N.H. Irving, deals with another outstandingly interesting aspect of chemistry, the experimental techniques by which the nature and composition of specimens are determined, that is to say, analytical chemistry.

In a limited space it has not seemed wise to illustrate more than incidentally the social significance of particular techniques, but there is a fascinating story in the evolution of the experimental methods themselves.

It becomes clear that, in spite of the apparently radical differences between old and new methods, there has been a certain constancy in men's attitudes to the material world as exemplified in both the antecedents of science and modern science itself. Since ancient times, men have developed theories of the constitution of matter in general. At the same time they have also developed methods of determining the composition of particular specimens of matter, for interest, for use, for effective control, or for commercial gain. This activity is what we now call *analytical chemistry.* This is a modern term but the basic idea goes back to the beginning of civilised life.

There are four ways of determining the composition of a specimen of matter:

(a) by isolation of a recognizable species;
(b) by comparison with one or more features of a sample of known composition;
(c) by inference from a chemical reaction;
(d) by inference from a physical characteristic.

Every one of the tests and measurements described by Professor Irving falls into one or other of these categories.

Analytical chemistry, may sound an unromantic pursuit. But if it does, please reflect that some techniques of analytical chemistry can help to determine that a loved one in the grip of an obscure disease may yet live, while others may reveal the composition of a remote star. Then this most far-reaching science will be seen to touch personal things and universal things. Looked at this way analytical chemistry will be seen to justify the devotion it has inspired in the generations of discoverers whose names are found in these pages.

Frank Greenaway
Keeper, Department of Chemistry

Technology & Testing: the first steps

As Society has become more organised and standards of living have changed and improved, analytical chemistry has become increasingly important and its influence extends over every aspect of our life. It is an essential feature of all manufacturing operations from the examination of the raw materials to the finished products and it dominates all problems involving the control of environmental pollution. It plays an ever increasing role in controlling the content and quality of the food we eat; it influences the vessels we cook with, the plates we eat off, the houses we live in, the clothes we wear, and even our modes of transport, education and entertainment - although the connections may not be immediately obvious. The medicines we use in ever increasing numbers could not be designed, tested, manufactured or distributed without the aid of analytical chemistry. The constant battle against fraud and crime - whether it be the adulteration of foodstuffs, the forging of documents, the doping of racehorses or athletes, or the investigation of road accidents and crimes of violence - all call on the skill of the analyst.

If analytical chemistry is involved in so many activities, what common feature can we find to describe its basic functions? For the moment let us agree that it exists to answer the question "What's in it - and how much?", realizing that the specific question and the amount of detail required in answering it must vary from case to case. Some of these questions can be answered easily and quickly; others tax to the limit the skill and resources of the most highly trained scientists.

The origins of analytical chemistry

It is something of a paradox that analytical chemistry of a sort was most certainly practised long before the science of chemistry, as we know it today, came into being. Indeed, it was only by repeatedly putting and answering the question "What's in it - and how much?" that successive generations amassed the basic facts which, when properly assembled and interpreted, formed the foundations on which the organised science of chemistry could be built. It is also something of a paradox that as the questions put to the analytical chemist have become more complex and sophisticated, and harder to answer in terms of the time and money available, increasing use has been made of physical methods of analysis, so that many of the problems put to the analytical chemist are now solved without recourse to any changes in chemical composition.

From the beginning of recorded history civilised man has adapted the material provided by Nature to his own purposes. The ability to make vessels of metal, pottery and glass, to tan animal skins and dye fabrics, to make soap, perfumes and cosmetics, and to preserve foodstuffs existed for many centuries before Christ. The ancients distinguished various ores and minerals and knew how to obtain the metals gold, silver, copper, iron, tin, lead and mercury, and how to prepare a variety of alloys. Soda, saltpetre and rock salt were readily obtainable. Potash could be prepared from vegetable ashes. Lime could be made by heating chalk or limestone, and the lime could be used to convert soda or potash to caustic soda or caustic potash. Vitriols were known (glassy crystals, hence their name, of iron or copper sulphate). Vinegar (acetic acid) was the only acid known in early times.

All these substances were handled by craftsmen who specialised in particular trades and who jealously guarded their "trade secrets". Although the basic operations of distillation, evaporation, crystallization and filtration were well established by the third and fourth century AD it must be emphasised that this widespread use of what is essentially chemical technology was carried on long before chemistry, as we now know it, became a science.

Early assaying of precious metals

Nevertheless, the problem "What's in it - and how much?" recurred from the earliest times. In view of the intrinsic value of gold and silver and their use in coins, jewellery and precious vessels, the control of their purity became a matter of importance in order to detect fraud and to defeat the activities of counterfeiters. In the absence of mineral acids only 'dry' methods could be employed and it is quite remarkable that the earliest analytical procedure, that of fire-assay or cupellation, is still in use today. References to fire-assay were found in cuneiform tablets. We read that the King of Babylon complained to the Egyptian Pharaoh Amenophis the Fourth (1375 - 1350 BC) "Your Majesty did not look at the gold which was sent me last time . . . after putting them into the furnace this gold was less than its weight". The Bible contains several references to fire-assaying, such as "I . . . will refine them as silver is refined and try them as gold is tried", "As they gather silver and brass, and iron, and lead, and tin, into the midst of the furnace, to blow the fire upon it, to melt it . . .", or "And I will turn my hand upon thee, and purely purge away thy dross, and take away all thy tin . . .".

The process of fire-assay is essentially quantitative in that it depends upon the change in weight before and after some appropriate heat treatment. The necessary balance was a familiar piece of equipment that had been known and used from very early times; indeed weights used in Babylon in 2600 BC still survive.

The separation of silver from gold was a difficult task. Pliny refers to a chemical method in which the suspect gold is roasted with salt and iron sulphate in the presence of brick dust which absorbs the silver chloride formed and leaves pure gold. However some 250 years earlier Hieron, King of Syracuse (200 BC) who suspected that his goldsmith had charged him the full price of gold for a new crown that might have been made from a gold-silver alloy, asked Archimedes to determine its true composition. As every schoolboy knows, Archimedes determined the density of the crown by making use of the fact that a body immersed in fluid is buoyed up by the amount of fluid it displaces. Since the density of gold (19.3) is nearly twice that of silver (10.5) the composition of the crown could be determined by a purely physical method and the crown itself suffered no damage.

One of the earliest references to a reaction in solution is again recorded by Pliny who states that the adulteration of copper sulphate by iron sulphate could be detected by testing a solution with a strip of papyrus soaked in an extract of gall-nuts, which became black if iron was present. This test can be regarded as the forerunner of innumerable colorimetric procedures in use today.

The history of Europe in the first centuries of the present era reflected the collapse of the Western Roman Empire and the subsequent influence of the Byzantine emperors under whose rule trade and industry flourished, libraries were founded, and study was encouraged. The Arab invasion of the eight century led to Islamic domination in Mesopotamia, Syria and Egypt, some of the learning of the ancient civilisations survived and, indeed, so influenced the new rulers that science and education began to flourish and in turn profoundly influenced Christian Europe.

During this period and through the Middle Ages there existed, alongside the practical chemistry which aimed at producing useful substances, a chemistry-based philosophical system known as alchemy. It attempted to prepare gold and silver from base elements such as lead, not primarily for profit but in order to throw light on ways of improving the human soul. In the course of innumerable experiments to these ends a great deal of new chemical knowledge came to light from the activities of Greek and, later, Arabian alchemists: this knowledge was further extended by Christian alchemists in later centuries.

Assaying for gold remained a most important practical analytical procedure and in the *Summa perfectionis magisterii* written in the thirteenth century (over the name of Geber, dubiously identified with the Arabian alchemist and physician Jabir Ibn Hayyan who lived in the eight or ninth century) the procedure is clearly described in detail together with accounts of the preparation of sulphuric acid by distilling alum, and nitric acid from vitriol, saltpetre and alum. Nitric acid (aqua fortis) was known to dissolve silver but not gold and became extensively used for separating the two metals: *aqua regia,* prepared from nitric acid and ammonium chloride, dissolved even gold and precipitated any silver as its insoluble chloride.

By the fourteenth century cupellation had become a statutory method for examining gold and Charles 1 of Hungary decreed in 1342 that a special laboratory *(domus regalis)* should be set up in every mining town for this purpose. Disputes between the results obtained by the official analyst and the tester elected by the citizens themselves were not uncommon, because they used somewhat different procedures. Similar problems persist to this day in all fields of analytical chemistry and constant efforts are made to secure agreement on detailed procedures and results by extensive inter-laboratory testing, nowadays on an international scale.

Early developments in technical analysis

Although during the fifteenth to seventeenth centuries zinc, antimony, bismuth and probably cobalt were discovered, together with many new reactions taking place in solution, there was still no true science of chemistry. One step in this direction was the development of "iatrochemistry" during the Renaissance period in Europe. This study of the application of chemical ideas to the making and usages of medicines originated in the works of Paracelsus (1493 - 1541).

Although many of the theories of the iatrochemists were as unscientific as much of alchemy, the development of chemistry and medicine drew closer together. The need to know more about the medicinal qualities of various mineral waters for example led to their being examined in great detail, special attention being paid to the solids left on evaporation and even to the gases evolved on heating. J.B. Van Helmont (1577 - 1644) was one of the first to recognise the existence of gases other than ordinary air.

During such studies many of the reactions now used in qualitative analysis were discovered. For example, A. Libavius (1540 - 1616) noted how the ammonia contained in water could be determined by the blue colour formed with a copper salt. He also showed that it was possible to distinguish alum, vitriol and saltpetre from the shapes of the crystals that separated from a saturated solution. Robert Boyle's book *Memoirs of a history of mineral waters* published in 1685 contained many new observations on organic reagents for metals and he used an extract of violets to distinguish acids from alkalis, which turned it green: this is the first reference to an acidimetric indicator. He was also the first to use a solution of hydrogen sulphide (prepared very indirectly from flowers of sulphur, potash and ammonium chloride) as an analytical reagent and noted the black precipitate it formed with lead, gold and mercury, and the yellow-brown precipitate with tin. Friedrich Hoffman (1660 - 1743), Professor of Medicine at Halle, Germany also wrote an important book on the examination of waters and discovered the presence of magnesium salts and how to distinguish them from calcium salts.

The emergence scientific chemistry

During the seventeenth and eighteenth centuries such discoveries followed thick and fast and the time was rapidly approaching when all new material could be organised into the science of chemistry. Robert Boyle's description "I call elements those primary and simple bodies, which do not contain anything, cannot be made from one another, form complex bodies, and into which complex bodies can be reduced" (1661) is remarkably close to the modern definition (at least until recent atomic theories). The quantitative study of the composition of alkalis by Joseph Black, the discovery of oxygen (1774) and other gases by Joseph Priestley (1773 - 1804) and quantitative studies of combustion and respiration by Antoine Lavoisier (1743 - 1794) are a few of the factors which made possible a systematic co-ordination of chemical facts, and a general theory of elements and compounds. John Dalton's theory (1803 - 1808), which some people regard as the foundation of modern chemical theory, gave a common numerical basis to the laws of conservation of mass, constant composition and multiple proportions, which were implicit in the work of many experimental chemists. Wenzel for example published a book which recorded the composition of some two hundred salts with great accuracy (for the time). Extensive and careful work by analysts was linked to the common theory of atomic weights. Chemistry as an independent science ultimately relies on the work of the analyst linked with a fundamental theory of composition. This is equally true in the most advanced research and in the most humdrum of routine chemical work.

It was pointed out earlier that chemical analysis came into being to meet the demands of early technology. During the eighteenth century the need for metals increased rapidly and iron, in particular, was needed in quantity as small scale processes were superseded by industrialised production methods. Increases in iron smelting created a shortage of wood and charcoal which led to its replacement by coal. Unfortunately the reduction of iron ores with coal yielded an inferior, brittle product; it was not until about 1750 that careful analytical work began to show the differences in coals and ores that led to differences in the iron produced from them. The increased demand for iron ore and for coal led to extensive developments in mining, and the need to overcome the problems of drainage and the hazards of flooding were first met by water pumps driven by steam power. The development of a more efficient steam engine by James Watt in 1769 led in turn to a greater need for iron for engines and machines, such as the spinning frames and power looms of the new textile industries.

More mining led to the discovery of new minerals and this created fresh problems for the analysts of the period and many new methods began to be developed, quantitative as well as qualitative. It is not surprising that those countries with the richest ore mines, such as Sweden, should become centres for the developing science of analytical chemistry, and metallurgists and even miners came to replace medically trained men as exponents of the art. Sweden led the world in metallurgical analysis until about 1875 although one cannot underestimate the contributions of R. Kirwan (1735 - 1812) in Great Britain, M.L. Klaproth (1743 - 1817) in Germany and L.N. Vauquelin (1763 - 1829) in France. Existing techniques were developed and led to the discovery of new elements such as uranium, zirconium and cerium, while extending the detailed knowledge of the alkaline earths and of tellurium, titanium and chromium. Klaproth's publications were immensely important in that, unlike many of his predecessors, he gave the most meticulous details of his analytical procedures and all the relevant numerical data. He originated the technique of alkali fusion for opening up minerals and used silver and platinum vessels for this purpose. He realised that foreign material could be introduced into his samples when they were finely ground in a mortar - and made the appropriate corrections. He realised that precipitates must be dried to constant weight and made striking advances in the quantitative analysis of mixtures of iron, manganese, aluminium and chrominium in solutions containing phosphate and arsenic.

Berzelius & the blow-pipe

Despite such achievements, the dominating figure and perhaps one should add the most autocratic figure of the early nineteenth century was the Swedish scientist J.J. Berzelius (1779 - 1848) who not only described his own remarkable achievements in a series of annual volumes, the *Jahresberichte,* which appeared regularly for twenty-seven years and were translated into English, French and German, but was also the author of books on electrochemistry (1814), mineralogy (1819), the use of the blow-pipe (1820) and of a very influential textbook of chemistry (1836).

Besides making a long and authoritative series of precise measurements of atomic weights (relative atomic masses), work which involved great originality in both qualitative and quantitative analytical chemistry, Berzelius discovered in the course of his work several new elements. Moreover he trained in his laboratory others such as E. Mitscherlich, V. Rose, F. Wöhler and H.G. Magnus who became eminent as analysts in their turn. It seems remarkable that such epoch-making work was conducted in a laboratory which Wöhler described as "consisting of two ordinary rooms . . . with neither a furnace, hood, water nor gas in it . . . . On the walls there were a few shelves with reagents on them and in the middle . . . a glass-blowing table and a large cupboard containing instruments. In the kitchen . . . there was a small furnace, seldom used, and a sand-bath which was kept continuously heated".

At this period, most vessels and apparatus were made of glass and Berzelius made most of his own apparatus and indeed invented such now familiar articles as the test-tube and separating funnel.

Mention ought now to be made of an important analytical technique namely the use of the blow-pipe, clearly derived from a scaling down of metallurgical operations. It was an indispensable adjunct to the qualitative examination of minerals during the eighteenth and nineteenth centuries for it had the special advantage of being rapid, needing only small samples, and capable of being used in the field by prospectors. Once a feature of every course of instruction in qualitative analysis, it has fallen out of use since the first decade of the present century.

Goldsmiths and glass-blowers had used a blow-pipe, so the technique was not itself novel. But in the mid eighteenth century Gahn and Cronstedt adapted it to give a fine and concentrated conical flame which could be directed on to a small powdered sample contained in a depression hollowed out of a block of charcoal. This innovation effectively reduced metallurgical operations from furnace scale to pinhead scale, and raised the temperature which could be attained very considerably. At the high temperatures so obtained materials could be melted and metallic oxides reduced, a process assisted by the addition of "fluxes" (soda, borax, or "microcosmic salt" [sodium ammonium phosphate]). A practised exponent could gain much valuable information from the colour and reactions of the residue or metallic bead formed by certain metals. Bergman, one of the greatest analysts of the eighteenth century summarised all the available knowledge of blow-pipe practice in his book *De tubo feruminatorio* (1779). Berzelius's book *Abhandlung om Blasrörets an-*

wendande i kemien och mineralogien (1820) contained little additional information but it served to disseminate detailed knowledge of the technique through its translations into many European languages.

It is scarcely surprising that analytical chemistry, inorganic chemistry and mineralogy were virtually inseparable during this period of growth. Quantitative determinations were characterised by the progressive refinements and elaboration of gravimetric analysis in which each component of a complex mixture has to be separated completely from every other substance, obtained from solution in the form of a chemical compound of reproducible and known composition, collected and weighed when completely dry. Patience, sustained concentration, a high degree of manipulative skill and even qualities of integrity are needed when carrying out the quantitative gravimetric analysis of, for example, a mineral, even when the full details of procedure have been previously worked out. Not everyone has or can acquire such personal qualities and a history of analytical chemistry could well be written in terms of the attempts made to simplify the various procedures of a quantitative analysis, to shorten the time needed, and to make the tasks accessible to less highly skilled technical assistants.

A move in this direction had started even by the middle of the eighteenth century and once again the new analytical procedure, that of volumetric (titrimetric) analysis, was developed to meet the requirements of industry, in this case the textile industry that had developed in England and France. Since manufacturers had to purchase the basic chemicals - sulphuric acid, soda, hydrochloric acid and chlorine water - from others, the quality of these materials became a matter of real concern. While the strength of soda was important to the soap manufacturer, the textile manufacturer needed to know the strength of hypochlorite solution "Pour prevenir tous les accidens qui peuvent resulter de l'energie trop grande de la liqueur" as Berthollet wrote in 1789.

This problem was solved by F.A.H. Descroizilles (1757 - 1825) and his method, not published until 1789, was quite widely known some years earlier. A solution of indigo in concentrated sulphuric acid was added a little at a time to a fixed volume of the bleach solution (delivered by a measure, or pipette as we would now call it) until its blue colour persisted.

This was the first example of a redox titration, but it was certainly not the first case where the principle of titrimetric analysis had been used. According to E. Rancke-Madsen's book *The Development of Titrimetric Analysis till 1806* this occurred in 1729 when C.J. Geoffroy determined the strength of vinegar by taking a known weight and gradually adding solid potassium carbonate until effervescence ceased. The strength of the vinegar was then expressed in terms of the weight of this alkali needed. In 1747 L.G. Le Monnier compared the amounts of alkaline earth carbonates in a series of samples of identical weight from the number of drops of sulphuric acid consumed before effervescence ceased. F. Home (1756) determined the amount of alkali in pearl-ash in terms of the number of teaspoonfuls of dilute nitric acid needed before effervescence ceased. An important improvement was introduced by William Lewis (1767) who used the change in the colour of litmus to determine the endpoint, rather than the cessation of effervescence. Here the amount of hydrochloric acid required was determined by weighing the vial containing it before and after the titration. The acid itself was standardised against a known weight (⅛ oz) of pure potassium carbonate and diluted so that it required exactly 4 oz to neutralize this amount.

Descroizilles' procedure clearly represents a closer approach to present day methods and he made a further advance in devising a 'burette' to contain his standard solutions. This was a narrow, finely calibrated tube some 20-22 cm long and 1.4-1.6 cm in diameter with a lip at the top to assist pouring and a small hole to allow air to enter and in this way to control the outwards flow of titrant. In his method for determining commercial alkalis (1806) an extract of violets was spotted onto a glass plate and used as an external indicator to follow the course of neutralisation. Descroizilles also invented the standard volumetric flask which he described as "a small jug with a volume slightly greater than 2 dl, on the neck of which a mark is made with a diamond indicating the place up to which the vessel contains just 2 dl".

Of the very many scientists who contributed to the development of titrimetric analysis about this time special mention must be made of Joseph Louis Gay-Lussac (1778 - 1850) who exploited new reactions, developed the actual techniques and did much to popularise titrimetry in France as a convenient, rapid, and reasonably reliable method of analysis. From France this knowledge spread to other countries. Gay-Lussac's best known contribution arose from the current difficulties in assaying silver by cupellation which caused some laboratories to obtain consistently high and others consistently low results. Astute dealers soon found that they could make a useful profit by buying silver with a "low" assay and selling it again where they knew they could get a "high assay". In 1829 an embarrassed Administration asked Guy-Lussac to devise a simple and rapid procedure to give results with an error less than 4 to 5 parts in 10,000. The method he proposed was to titrate a solution of the silver in nitric acid with a standard solution of sodium chloride until such time as the next addition of a drop of diluted standard solution produced no further turbidity due to the precipitation of silver chloride. Such an analysis only took some 15 minutes. The only improvement of the basically simple procedures made in the following 150 years was the substitution of a potentiometric endpoint.

In 1841 T. Clark (1801 - 1867) worked out a method for determining the hardness of water whereby titration was carried out with a standard solution of soap until the foam obtained on shaking persisted for 5 minutes - a method which has only comparatively recently been replaced by complexim etry.

Although it is impossible here to give any real indication of the tremendous activity at this time it is noteworthy that 1846 saw the first use by Louis C. Barreswil of an alkaline solution of a copper salt for determining reducing sugars, while Berthet used potassium iodate to determine iodide and F. Margueritte introduced potassium permanganate for the titration of iron. This important method for iron cannot be used if hydrochloric acid is present because of the reaction between the acid and the permanganate. In 1851 F. Penny introduced a standard solution of potassium chromate for this purpose.

The first text-book on titrimetric analysis, by Karl Heinruch Schwarz (1824 - 1890), was published in 1853 under the title *Praktische Anleitung zu Massanalysen (Titrir-Methode)* and was succeeded two years later by a much more extensive treatment, the *Lehrbuch der chemisch-analytischen Titrirmethode* written by Friedrich Mohr (1806 - 1879). Mohr's book and his own original researches did a very great deal to establish titrimetric analysis as an indispensible laboratory procedure. Although the first burette with a tap at the bottom had been used by E.O. Henry in 1846 such taps were very prone to leak and Mohr himself introduced the familiar type of run-out burette with a fine jet attached by rubber tubing and controlled by a pinch-cock or glass bead. (The cork-borer, the calibrated pipette and the 'Liebig' condenser were also originated by him).

Space does not permit of any detailed account of the systematic development of titrimetric analysis over the last century for new reagents, reactions, and applications were - and still are - continually being introduced. Synthetic organic substances which changed colour over a narrow and known range of hydrogen ion concentration (pH indicators) had a profound influence on the development of acid-alkali titrations. Other organic substances, such as diphenylamine introduced by J. Knop in 1925 played a similar role for oxidation-reduction processes. Absorption indicators such as fluorescein, introduced by K. Fajans in 1923 are employed where a precipitate is formed: at the end-point the indicator is absorbed and the precipitate changes colour. Fluorescence indicators and chemiluminescence indicators have enjoyed a vogue though their uses are limited. Electrochemical methods for determining the endpoint in acid-alkali titrations followed the introduction around 1920 of the hydrogen electrode, the quinhydrone electrode (and more significantly the

glass electrode since, among other things, this could be used in the presence of strong oxidising and reducing agents and with substances that would 'poison' platinum electrodes). The silver-silver chloride electrode was used for titrating chloride ions and quite recently ion-selective electrodes have been devised for calcium and fluoride ions and for a variety of other cations and anions. (E. Pungor, 1964 -)

One enormous advantage of endpoint detection based upon changes of potential in a suitable cell is that this can be used to operate recording devices. A wide variety of automatic titrimeters have been developed in which either a graph of the titration is drawn as it actually proceeds or the flow of titrant through an electromagnetically operated valve is stopped automatically when the pre-set endpoint is reached: the result of the titration may be displayed digitally.

The most recent and revolutionary developments in titrimetric analysis date from 1940 when G. Schwarzenbach introduced new methods for determining the calcium and magnesium hardness of water by using an aminopolycarboxylic acid of which ethylenediaminetetraacetic acid, EDTA, is typical. The anion of this acid forms metal complexes, often of very high stability, with almost all metal cations save those of the heavier alkali metals. By using a buffer solution the reaction can be made to go to completion. Its progress can be followed by any method suitable for following changes in the concentration of free metal ions, as a solution of the titrant is run in. This is possible in many cases using metal electrodes but the dramatic breakthrough was the discovery of metallochromic indicators such as murexide and eriochrome black which can play the same role for metal cations that acid-alkali indicators do for hydrogen ions. One of the most valuable features of this new procedure of complexiметry (or chelatometry) is that it is not restricted to reactions in which there is a change of oxidation state or the formation of a precipitate or of a coloured product. By the exercise of much ingenuity procedures have been developed for the determination of most cations and anions, for alloys and complex mixtures, and even for organic substances such as alkaloids and drugs.

Parallel with developments in the various chemical reactions that can be made the basis of volumetric procedures there have been refinements in the apparatus available and changes in the scale of working. Burettes of total capacity 1-2 cm^3 and graduated at 0.01 cm^3 are commonplace and micrometer syringes have been widely used for dispensing small volumes with an accuracy of 0.00002 cm^3 or better when titrating a single drop of solution. Pipettes capable of delivering accurately volumes as small as 0.001 cm^3 are in routine use, especially for radio-chemical work.

Instead of preparing a standard solution of titrant containing a known weight of some highly purified reagent in an accurately known volume (or weight) of solution, a further development has been to generate the titrant *in situ* by electrolysis. In such coulometric titrations (L. Szebellédy and Z. Somogyi, 1938) the amount of titrant is now measured in terms of the number of coulombs of electricity consumed - or, if a constant current is employed, by the time taken to reach the endpoint.

Titrations need not, of course, be carried out solely in aqueous solution. Apparatus, procedures and indicators are now available for titrations in e.g. glacial acetic acid, pyridine, liquid ammonia and dimethylformamide. The determination of water itself, especially when dissolved in organic solvents, deserves special mention. Karl Fischer devised (1935) a novel method in which the sample is titrated with a solution of iodine, sulphur dioxide and excess pyridine in anhydrous methanol. At the endpoint the colour changes from yellowish to brown, but it is preferable to use the electrometric "dead stop endpoint" introduced by C.W. Faulk and A.T. Bawden in 1926.

Organic analysis

So far nothing has been said about the analysis of organic compounds and indeed little was known of their composition before the beginning of the nineteenth century. Van Helmont's experiments led to the conclusion that carbon dioxide and water formed during the combustion of organic compounds originated from their containing carbon and hydrogen and Lavoisier considered that they contained oxygen as well. The presence of nitrogen in animal extracts was established by C.L. Berthollet in 1786.

Lavoisier's pioneering attempts to analyse organic compounds quantitatively were not very successful and the first reasonably accurate results were obtained by J.L. Gay-Lussac and L.J. Thenard in 1810. They heated the sample with potassium chlorate and measured the volume of carbon dioxide formed by absorption with potassium hydroxide. The excess of oxygen was determined from the decrease in volume after exploding with excess hydrogen. Clearly this hazardous process could not produce accurate results at all if the sample itself contained oxygen. J.J. Berzelius (1817) improved on this procedure and made the important innovation of weighing the water formed, and Gay-Lussac replaced the oxidant potassium chlorate by the copper oxide now used.

The essential basis of the modern combustion method stems from J. Liebig (1803-1873) who weighed both the carbon dioxide and the water formed after sweeping them out from the combustion tube with a stream of air. In compounds containing nitrogen the mixture of nitrogen and carbon dioxide produced in a separate determination was collected in a eudiometer and the volume of nitrogen measured after absorbing the carbon dioxide with potash. J.B. Dumas (1800-1884) made the rather obvious simplification of collecting the two gases directly in a eudiometer tube filled with potash and a further major improvement was the use of an azotometer which eliminated altogether the difficult transfer of gases from the combustion tube to a eudiometer.

Quite a different procedure for the determination of nitrogen was developed in 1883 by J.G. Kjeldahl who showed that organic compounds could be wet-oxidised by digestion with boiling sulphuric acid and potassium permanganate; on making alkaline, ammonia could be distilled out in steam and determined titrimetrically.

The determination of sulphur, halogens, phosphorus and arsenic can be effected by oxidising the sample with a mixture of sodium peroxide and potassium chlorate in a strong steel bomb, a method first used for samples of coal by Parr. However, the most widely used method is that developed by G.L. Carius during the period 1860-1870 in which the sample is heated with concentrated nitric acid in a stout sealed glass tube containing some barium chloride (for sulphur) or silver nitrate (for halogens). After cooling and washing out the contents, the barium sulphate (or silver halide) is collected and weighed. The direct determination of oxygen by transformation to carbon monoxide after heating with excess carbon to a high temperature forms the basis of several contemporary procedures.

Despite innumerable modifications and improvements in the details of procedure quantitative organic analysis remained a highly skilled and time-consuming operation until well into the 20th century, and one which demanded as much as 1 g of sample. With increasing

interest in natural products and synthetic laboratory products available only in very small amounts, and to service the newer sciences of biochemistry, biology and physiology, it became essential to scale down the whole procedure to permit of quantitative analyses with even only a few milligrams of material.

This achievement of this feat can be clearly attributed to Fritz Pregl (1869 - 1930). in 1910 the assay balance taking a load of 20 g was only sensitive to 0.01 mg. By October 1911, at Pregl's request, the instrument maker Kuhlmann of Hamburg had produced a prototype microbalance sensitive to 0.001 mg at the same loading and this enabled Pregl to develop his new microchemical procedures. These not only reduced the scale of operations with savings of time and material but, by a meticulous attention to even the tiniest detail of design and procedure, both the accuracy and the precision of quantitative organic analysis were increased.

Throughout this century there have been innumerable technical improvements - in all-electric and programmable heating of the combustion train, the nature of the packing and chemical absorbents, the use of quartz in place of hard glass combustion tubes and so on. By eliminating some of the slow weighing operations in favour of determining the amounts of carbon dioxide, water vapour and nitrogen formed by gas chromatography it has recently been possible to carry out a complete C, H and N analysis on a weighed sample quite automatically in some 15 minutes. In commercial apparatus the results appear directly as percentages on dials or even printed out on paper tape.

Specific & selective reagents

A landmark in analytical chemistry was the introduction of organic compounds as reagents for metals. M. Ilinsky (1884) and G. von Knorre (1885) noted that α-nitroso β-naphthol and β-nitroso-α-naphthol formed a stable cobalt salt $(C_{10}H_6ONO)_3Co$ which could be used for the determination of cobalt in the presence of nickel, though it also gave precipitates with a number of other elements. When L.H. Tschugaeff reported in 1905 that dimethylglyoxime formed a very insoluble red complex with nickel, of reproducible and stoichiometric composition, and that "one part in 400,000 parts of water is readily detected" (a reaction applied to the quantitative determination of nickel 2 years later by O. Brunck) a new era in gravimetric analysis commenced -- one in which organic reagents were used for the qualitative detection of small amounts of inorganic ions ('spot tests' - a field especially associated with the name of Fritz Feigl, born 1891) and for their quantitative determination by gravimetric and other methods. Dimethylglyoxime had the special virtue of giving an insoluble precipitate with nickel and palladium only. It was thus the first of the 'specific' (or more correctly, the highly 'selective') reagents for which a constant search is still being made in the hope of finding organic substances which would react with only one element or with a small number.

Cupferron, introduced by O. Baudische in 1909 acts as a precipitant for copper and iron in weakly acid solution. 8-Hydroxyquinoline, introduced by R. Berg in 1938, forms precipitates with quite a large number of metals but it can be made quite selective by a careful control of the pH and the presence of auxiliary (masking) agents. A feature common to many of the organic reagents is the favourably low 'gravimetric factor', i.e. the ratio of the weight of element to be determined to the weight of precipitate formed from it. In the determination of aluminium as the tris-8-hydroxyquinolinate this factor is 0.05872: in other terms 1 mg of aluminium would produce 17.3 mg of precipitate, thus permitting the gravimetric determination of quite small amounts without demanding an excessively sensitive balance.

Another feature of these metal complexes is that they are often strongly coloured -- thus lending themselves to absorptiometry (q.v.), or soluble in organic solvents immiscible with water -- thus permitting concentration by liquid-liquid extraction (q.v.). Some complexes fluoresce strongly in ultra-violet light and as little as one part per thousand million of beryllium can be detected, even when aluminium is present, through the intense green-yellow fluorescence produced by the organic reagent morin.

As pointed out by Irving in 1949, steric hindrance to co-ordination can be exploited to design organic reagents of increased selectivity. Thus 2-methyl-8-hydroxyquinoline will not give a precipitate with aluminium although, like 8-hydroxyquinoline itself, it still precipitates magnesium and beryllium, thus permitting some useful separations in the determination of light alloys. Biquinolyl is specific for copper (I) because steric reasons prevent its reaction with bivalent transition metal ions.

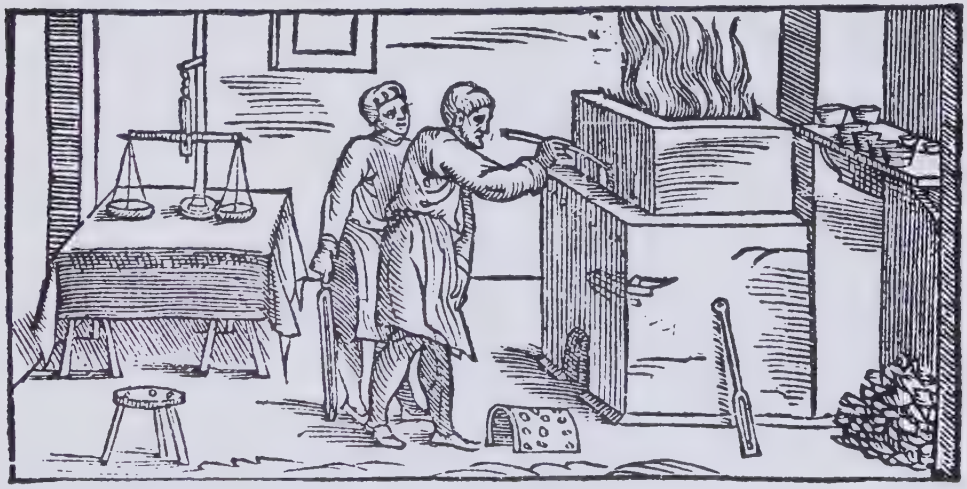
Physical methods of analysis

Any further history of the present widespread uses of organic reagents in inorganic analysis would occupy too much space and having now covered the early history of so-called 'classical methods' of analysis it is now appropriate to review those developments in physical methods of analysis which have been such a feature of the late nineteenth and present centuries. Although the results of some analyses can now be obtained without recourse to any of the purely chemical procedures referred to above we should never forget R. Chirnside's dictum "It is not so important to stress with Liebhavsky that the chemistry is going out of chemical analysis, but rather to emphasise that physics is coming in".

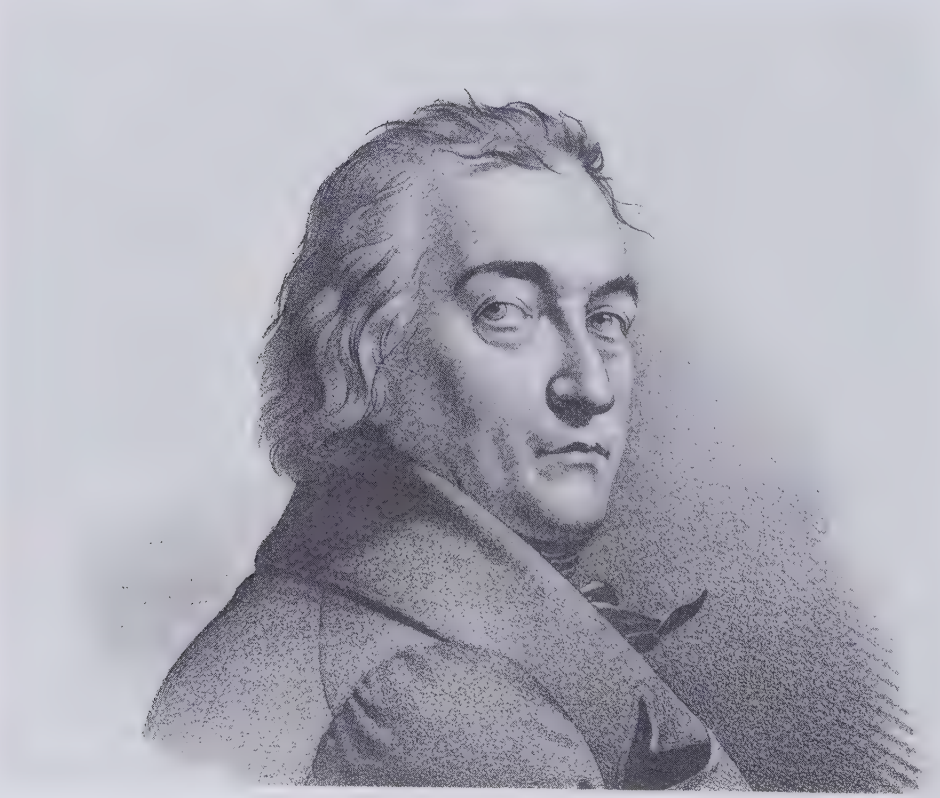
In many cases discoveries of new analytical procedures have been made simultaneously in different parts of the world. In most cases, however, the development and the constant redevelopment of a new technique results from many large or small advances in technique and instrumentation, progress in one field of endeavour reacting on and influencing others so strongly that considerations of priority and detailed chronology become increasingly difficult and even meaningless. Such problems arise from the very large number of scientists now involved in various aspects of analytical chemistry, the increased amount of interdisciplinary activity, the vastly improved speed of communicating new ideas and results, and the increasing role played by the manufacturers of sophisticated instruments (and their associated research staff) play in advertising and popularising new analytical procedures. In view of the limitations of space it would seem best to highlight certain main lines of development, dealing first with electrochemical phenomena, then with various aspects of spectra, followed by considerations of radiochemistry and the techniques of preconcentration and separation which lie at the basis of so many procedures in actual use.

1 Reconstruction of sixteenth century assayers' laboratory in the Chemistry Gallery of the Science Museum

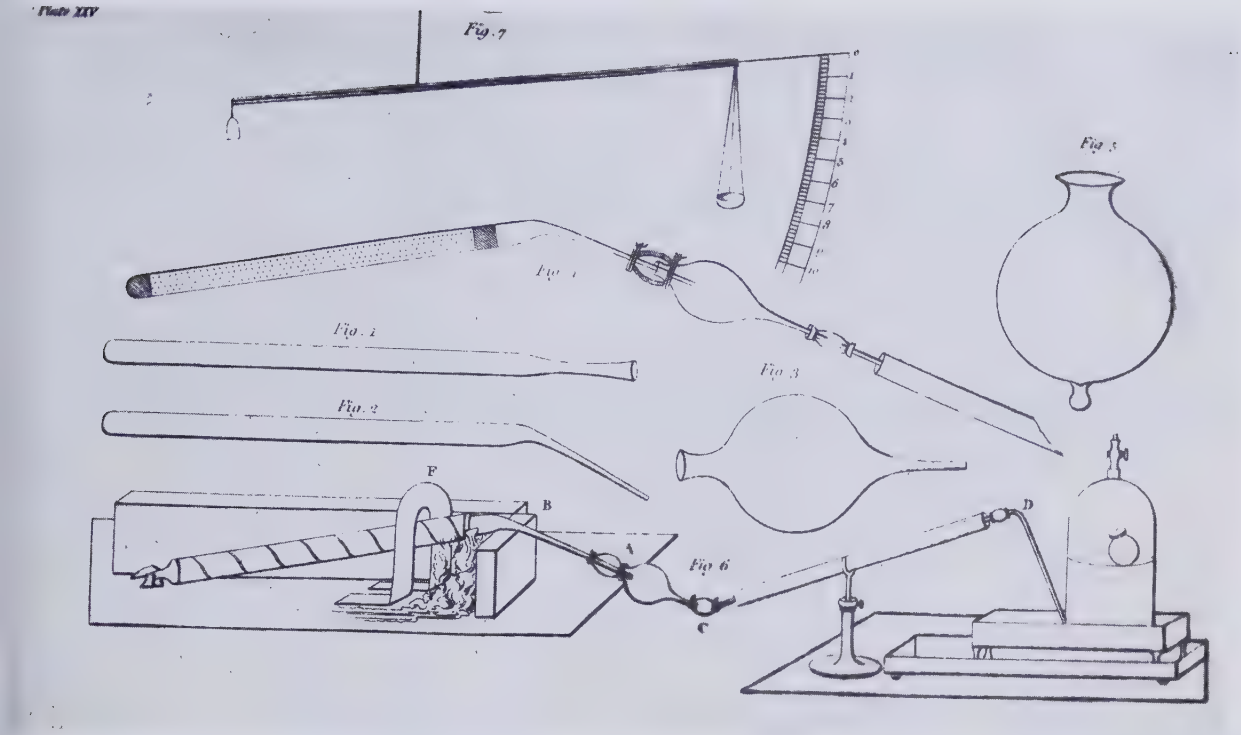
2 Assayers' laboratory showing balances, muffle furnace for cupelling, ingot mould (Biringuccio, 1540)



3 Carl Friedrich Wenzel
(1740-1793)

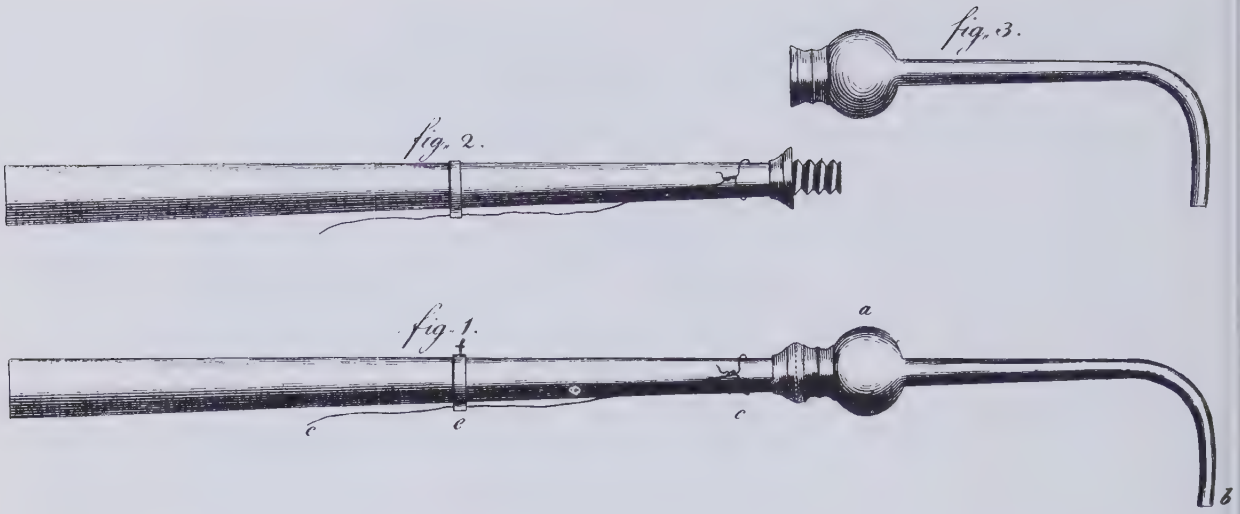


4 Claude Louis
Berthollet
(1748-1822)

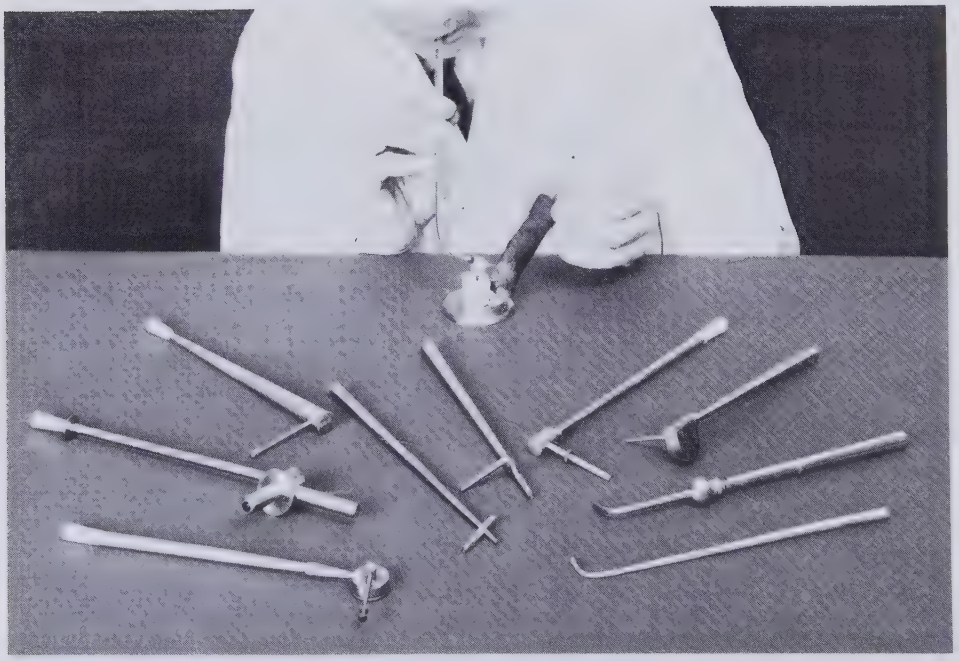


5 Berzelius's apparatus for organic analysis, 1814

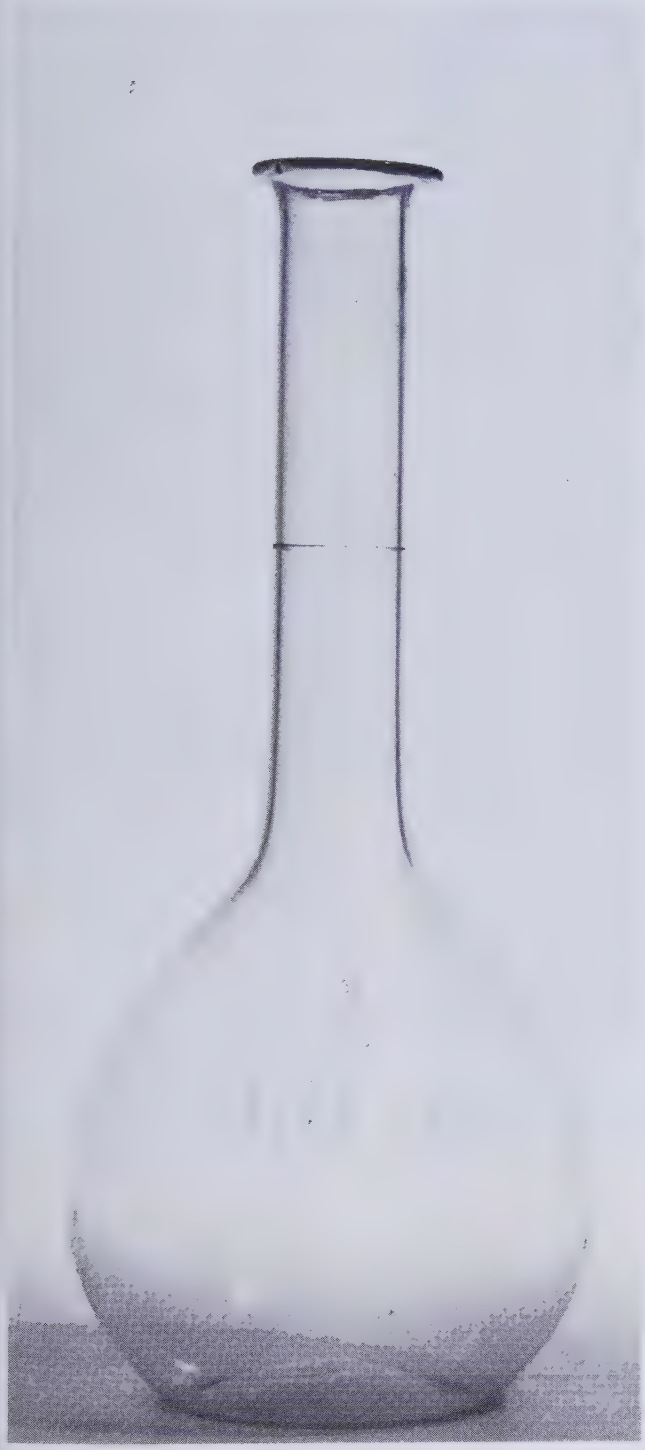
6 Jöns Jakob Berzelius (1779-1847)



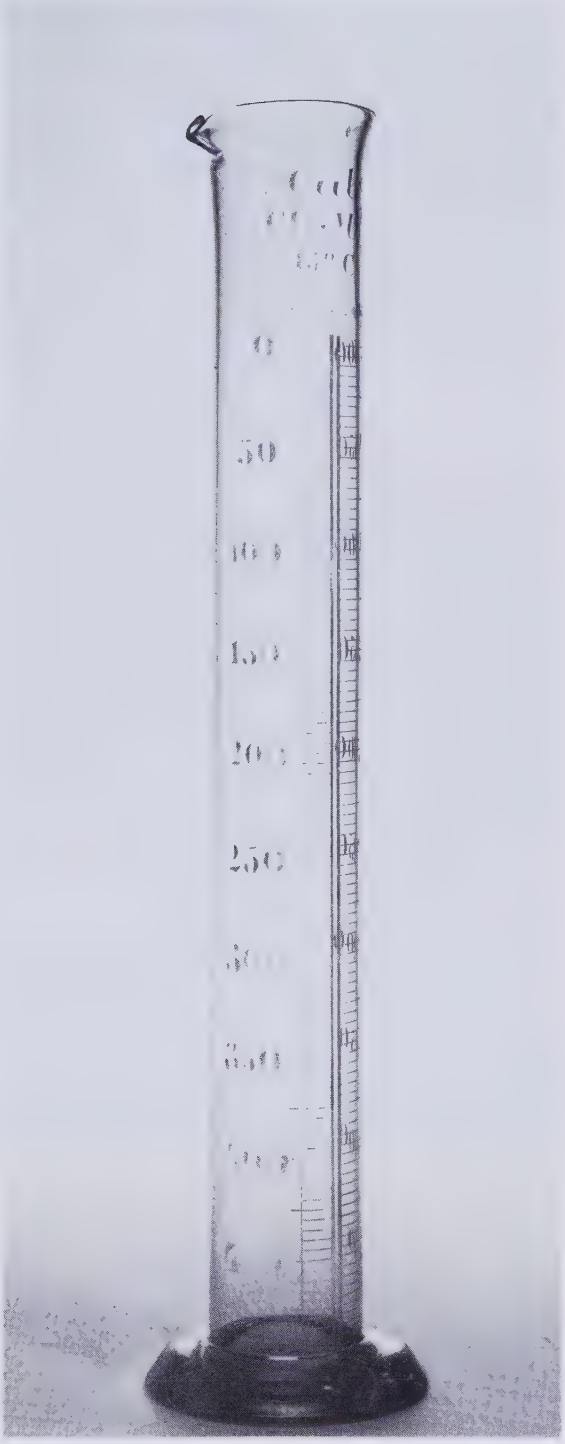
7 Cronstedt's blowpipe from his *Mineralogy*, 1758



8 Replicas of early blowpipes. Right to left: Simple mouth blowpipe and blowpipes by Cronstedt (1750, reproduced 1921), Bergman (about 1775, reproduced 1923), Gahn (reproduced 1915), Tennant (reproduced 1923), Wollaston (1806, reproduced 1923), Black (reproduced 1915), Bucknell (reproduced 1915), Pepys (about 1810)



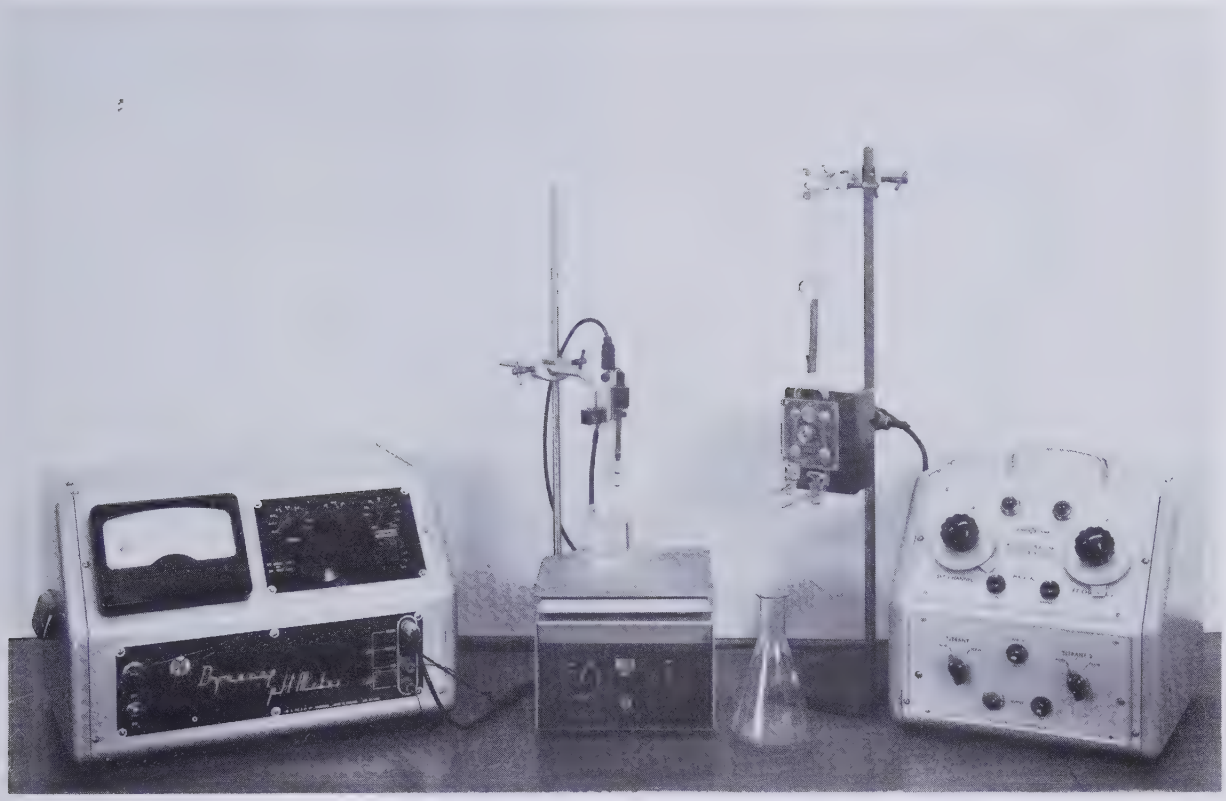
9 0·5 litre flask (1876)



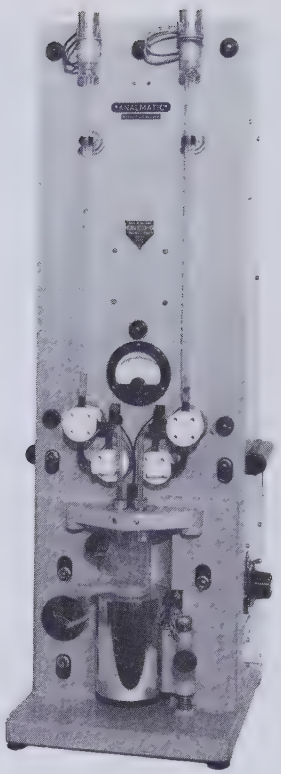
10 Graduated measuring cylinder about 1850

11 The first widely used burette, devised by Gay-Lussac (about 1830). Flow of liquid from the jet is controlled by a thumb placed over the other opening. The Binks burette is a modification of the Gay-Lussac type. Liquid flow from the delivery jet is controlled by a thumb over the side tube. One of Wollaston's scales of chemical equivalents (1814) is shown

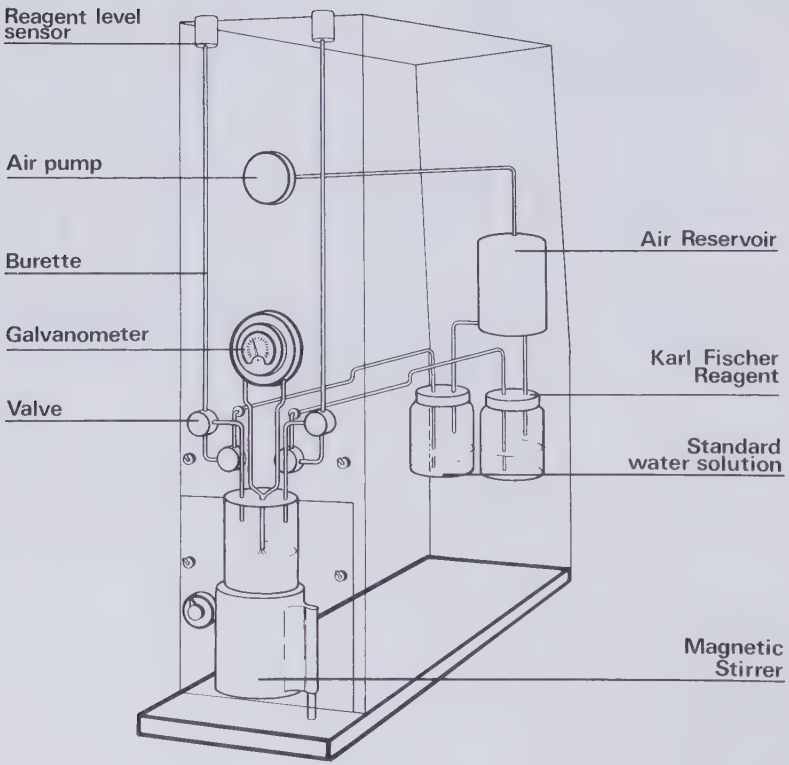
12 Burette (about 1850). This type of burette consisting of a straight tube with a tap at the bottom superseded the Gay-Lussac burette of the 1830s



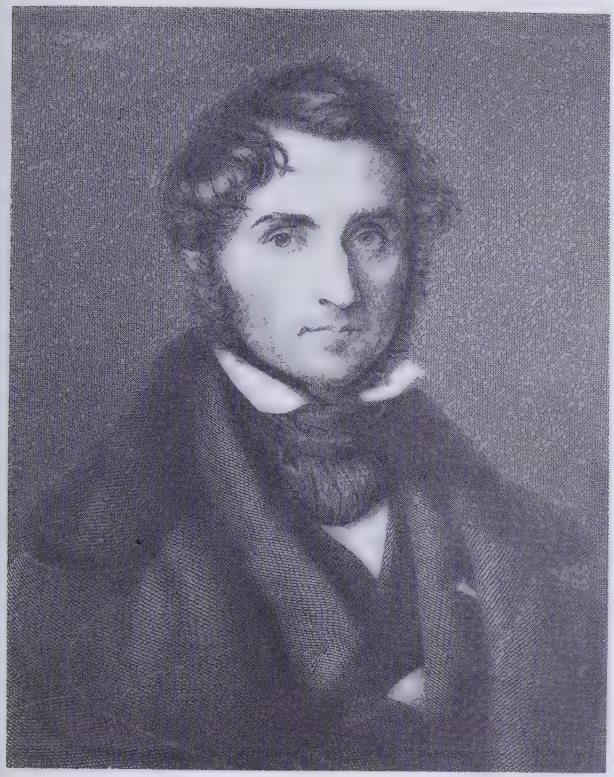
13 An autotitration apparatus employing a Dynacap pH meter (1962) connected to an autotitrator assembly. Electrodes connected to the pH meter dip into the solution to be titrated which may be heated and/or stirred by means of a stirrer hot plate assembly



14 An electrometric Karl-Fischer apparatus for the determination of water

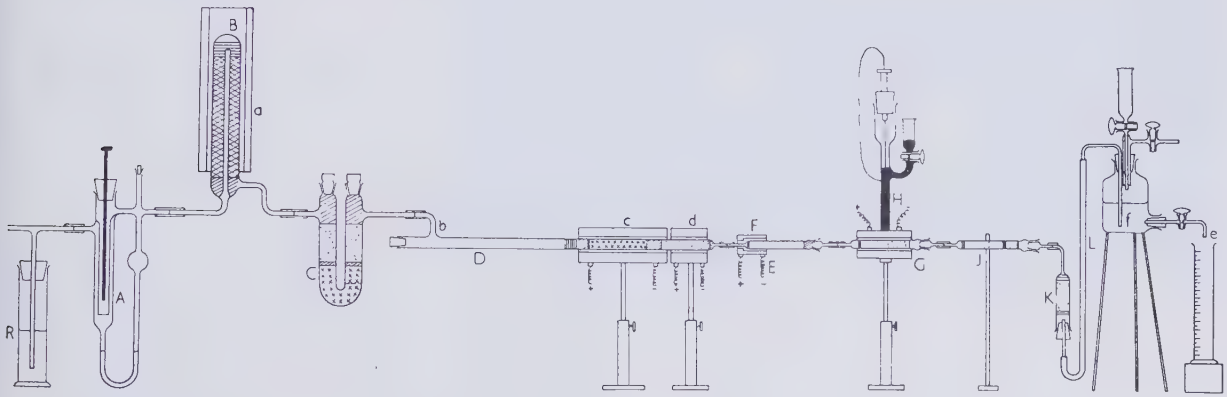


15 A schematic diagram of Karl Fischer electrometric apparatus



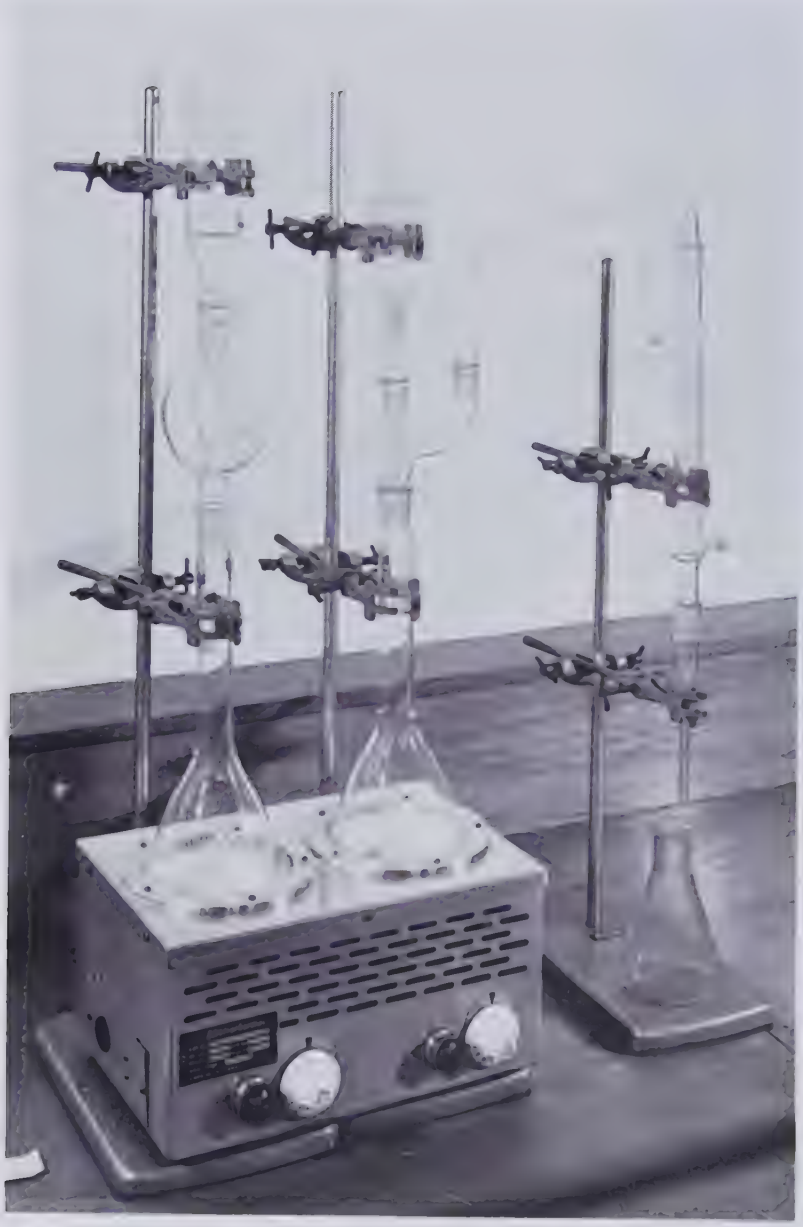
16 Justus Liebig (1803-1873)

17 Louis Jacques Thenard (1777-1857)



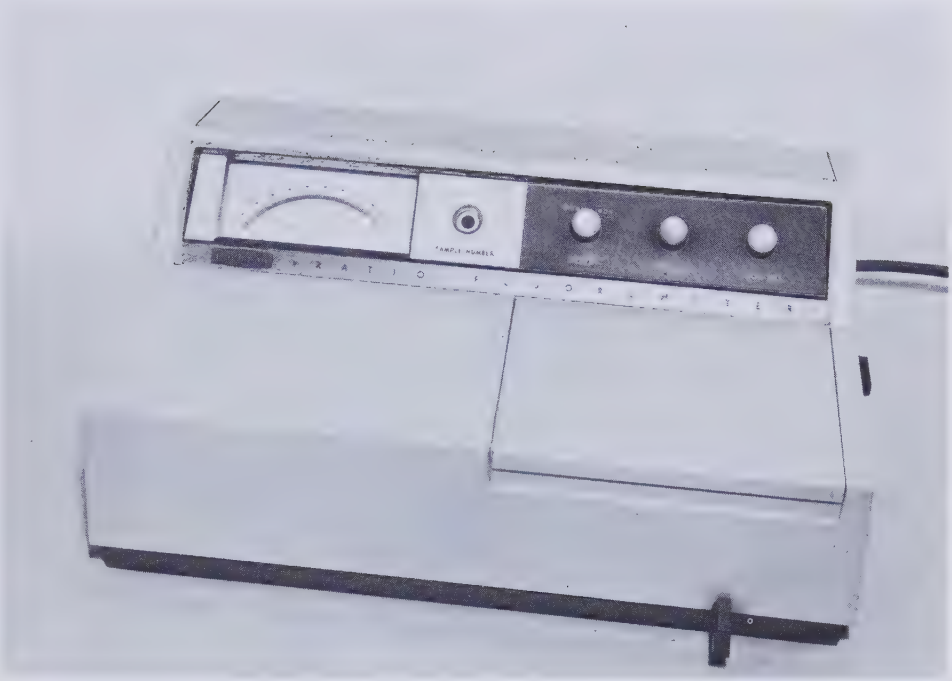
18 A typical modern combustion train for the determination of carbon and hydrogen as carbon dioxide and water respectively

19 Johann Gustaf Kjeldahl (1849-1900)

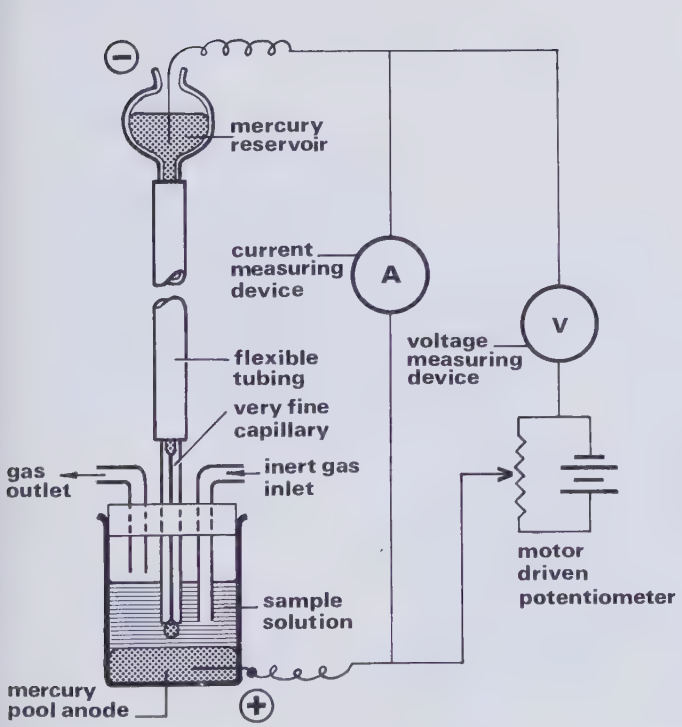


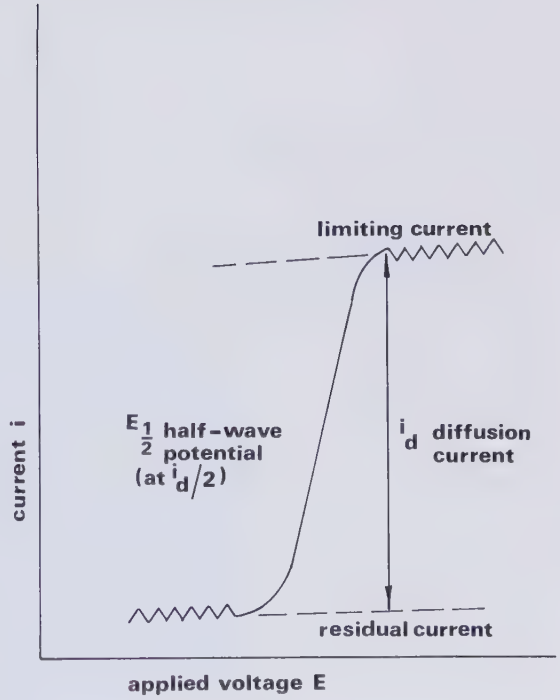
20 A modern Kjeldahl apparatus for the determination of nitrogen in organic compounds

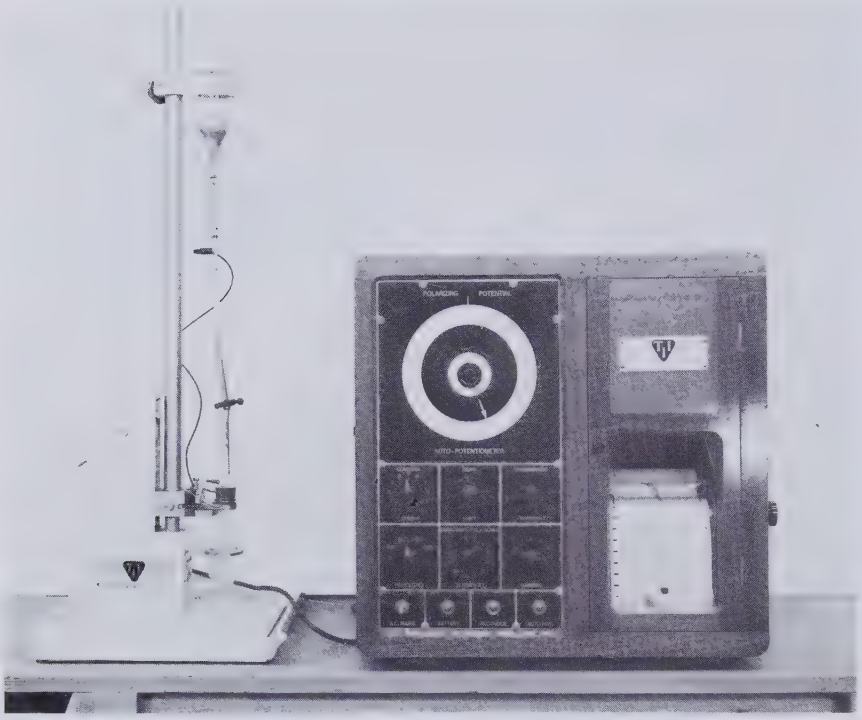
21 A ratio fluorimeter. Compounds which fluoresce under visible or ultraviolet light may be detected at very low concentrations, eg one part in a thousand million, and their concentrations determined in solution by the measurement of their fluorescence



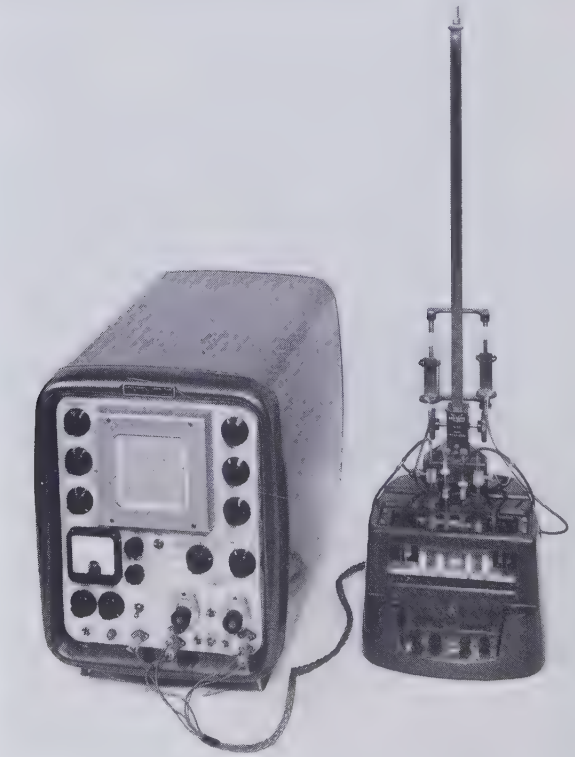
22 A schematic diagram of the operation of a polarograph showing
a) the dropping mercury electrode
b) a typical polarogram for lead







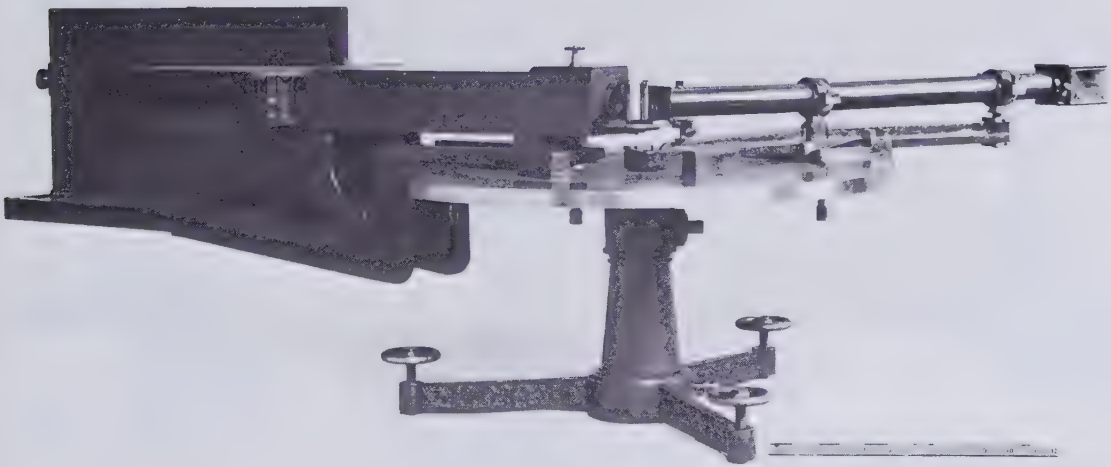
23 Tinsley polarograph. The polarograms are automatically recorded and displayed on a chart recorder

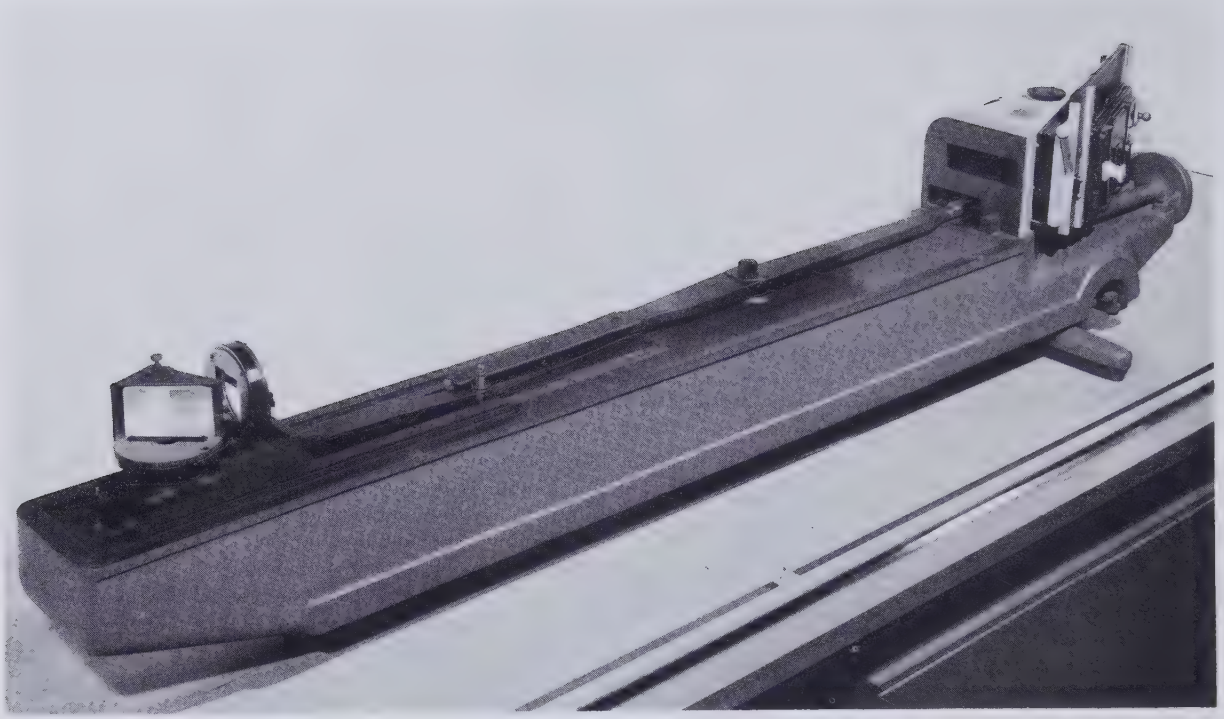


24 A Davis differential cathode ray polarograph. The polarogram appears as a trace on the oscillograph screen

25 Gustav Kirchhoff
(1824-1887)

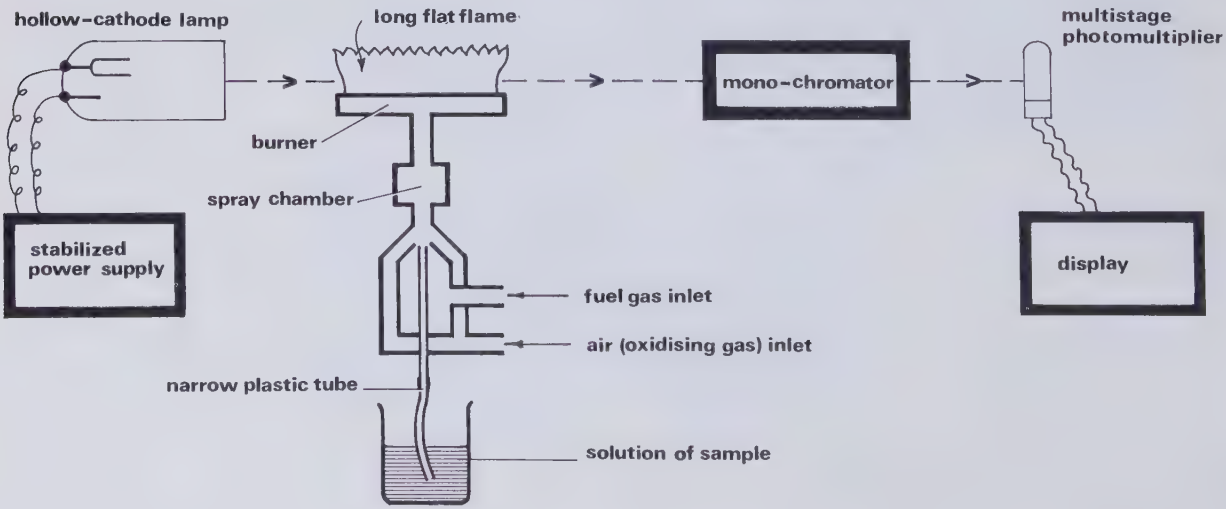
26 W.N.Hartley's original quartz spectrograph (1875). This had a quartz lens and a quartz prism so that ultraviolet, spark and absorption spectra could be obtained. The spectra were photographed on dry plates.



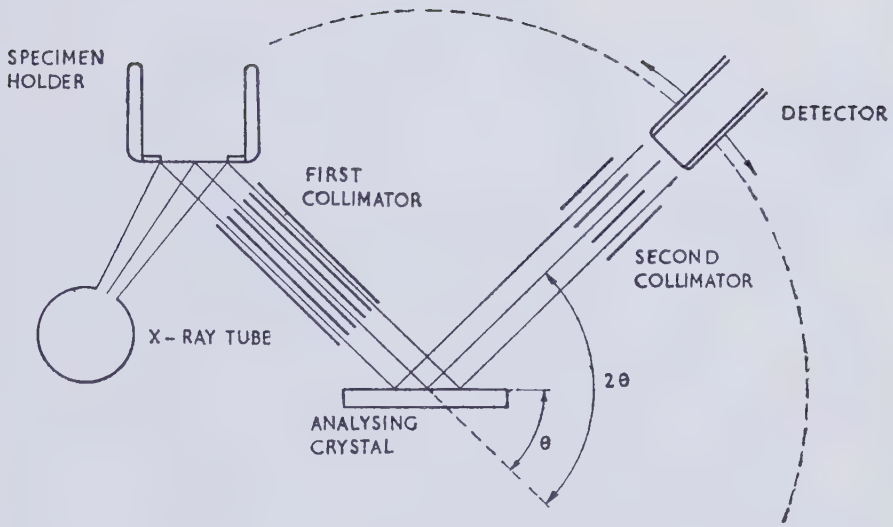


27 Hilger automatic large spectrograph (1965). All adjustments could be made using a single control. Quartz or glass optical systems could be employed. Its main use has been in the analysis of metals and alloys

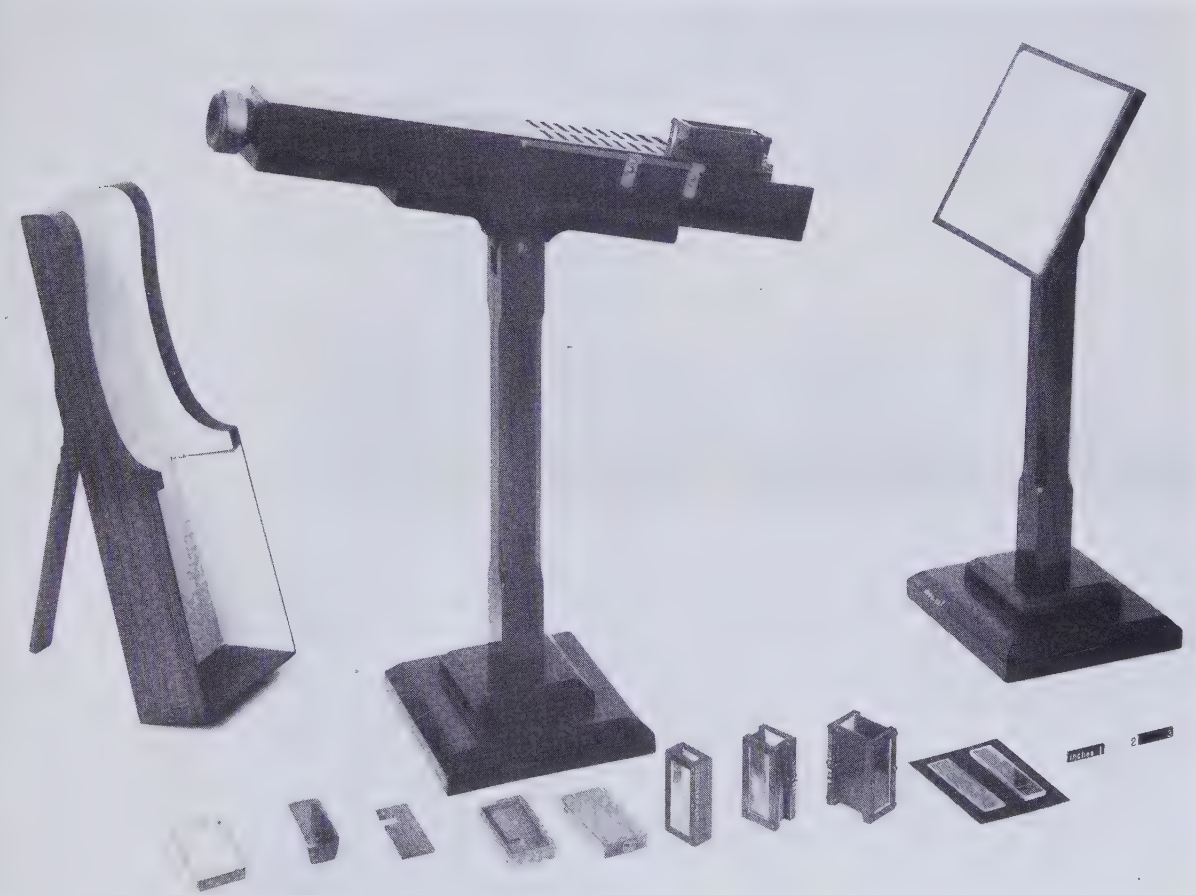
28 Diagram of experimental set-up for atomic absorption spectroscopy. Light from a particular element is produced by means of a hollow cathode lamp and passed through a flame containing atoms of the same element (from spray introduced with the gas stream). The light which has passed through the flame is dispensed by a monochromator and the amount absorbed by the analytical sample is indicated on a recorder or display unit



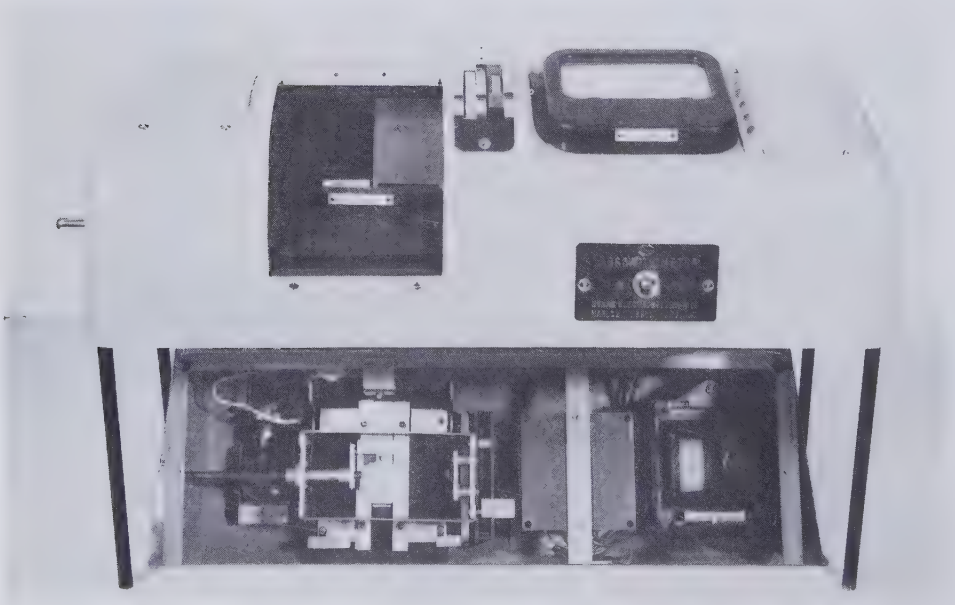
29 Diagram of experimental set-up for plane crystal X-ray fluorescence spectroscopy. X-rays from a source are directed on to a crystal specimen, passed through an analysing system and the X-ray fluorescence measured by a detector such as a Geiger-Müller counter or a scintillation counter



30 Tintometer, late nineteenth century, used for colour match-ing



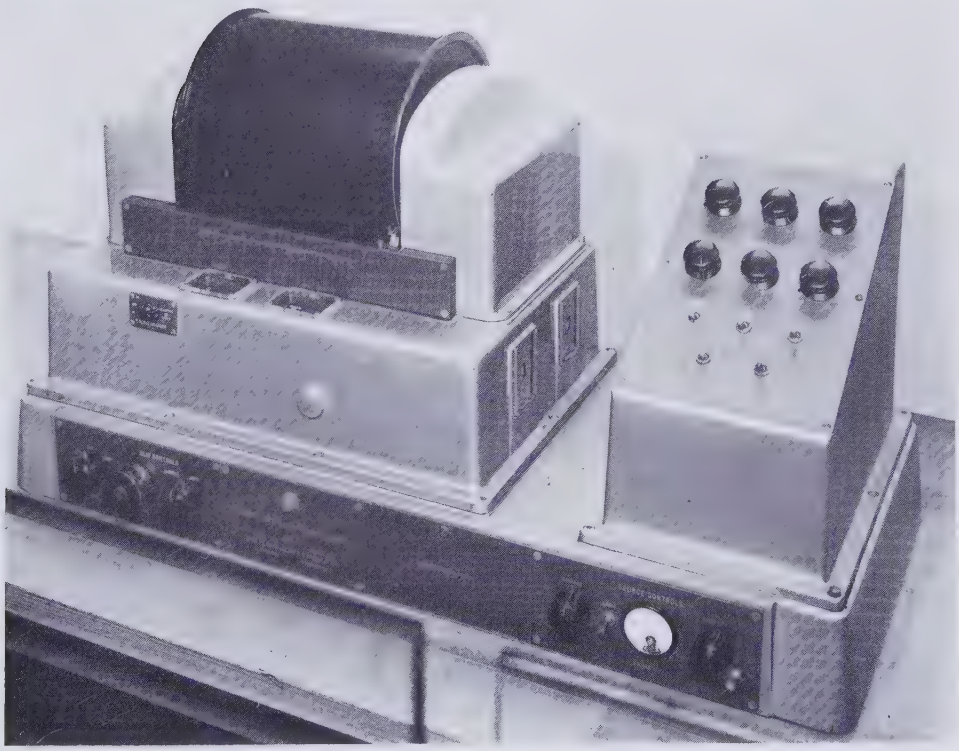
31 A photoelectric colorimeter used for simple colorimetric determinations. The instrument is manually operated (1965)

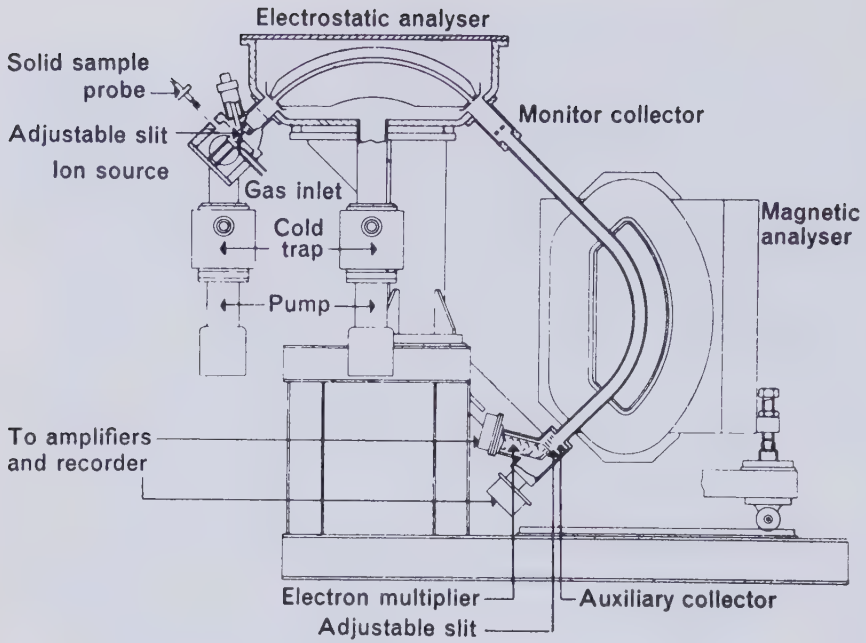


32 A photoelectric absorptiometer. The cell compartment and optical system have been exposed to show the working portions of the system (1954)

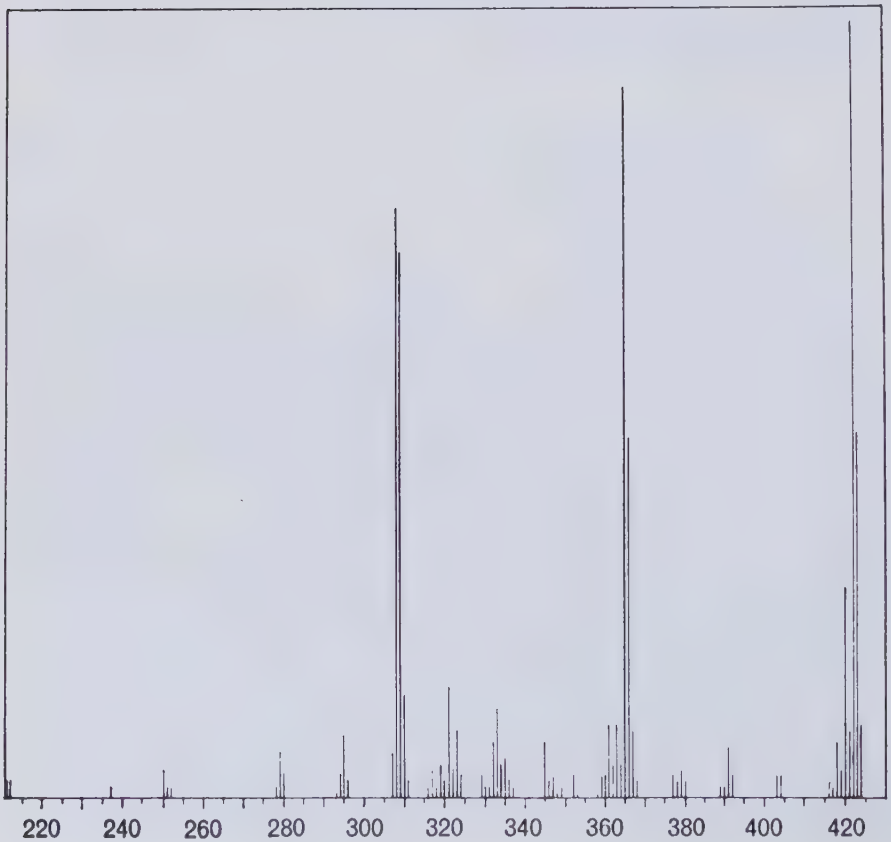
33 A photoelectric spectrophotometer. The instrument is used to plot visible and near ultraviolet spectra by hand (1965)

34 A double beam recording infra-red spectrophotometer for determining the groupings present in chemical compounds (1970)

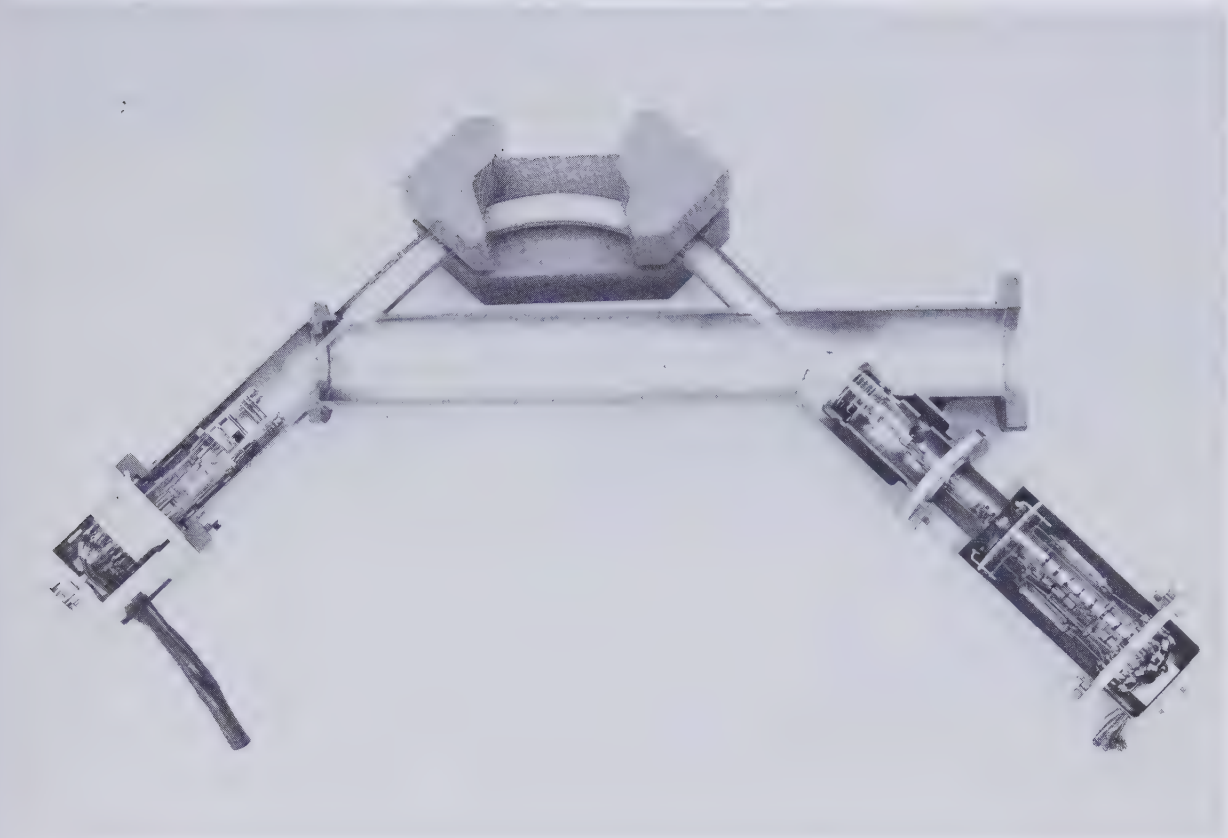




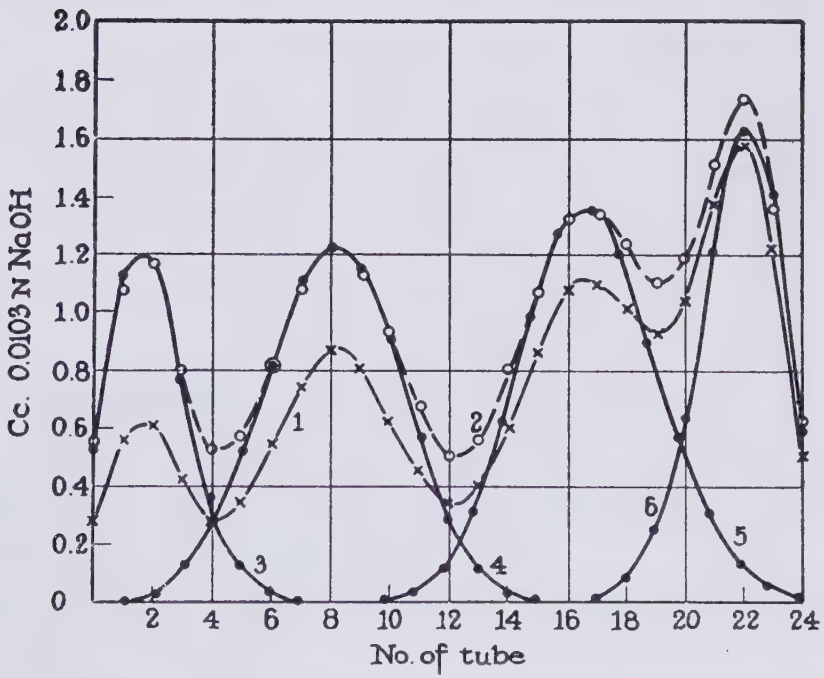
35a Schematic arrangement of the AEI MS 9 double focussing mass spectrometer. Spreading of the positive ion beam by collision with neutral molecules is made possible by use of a very high vacuum



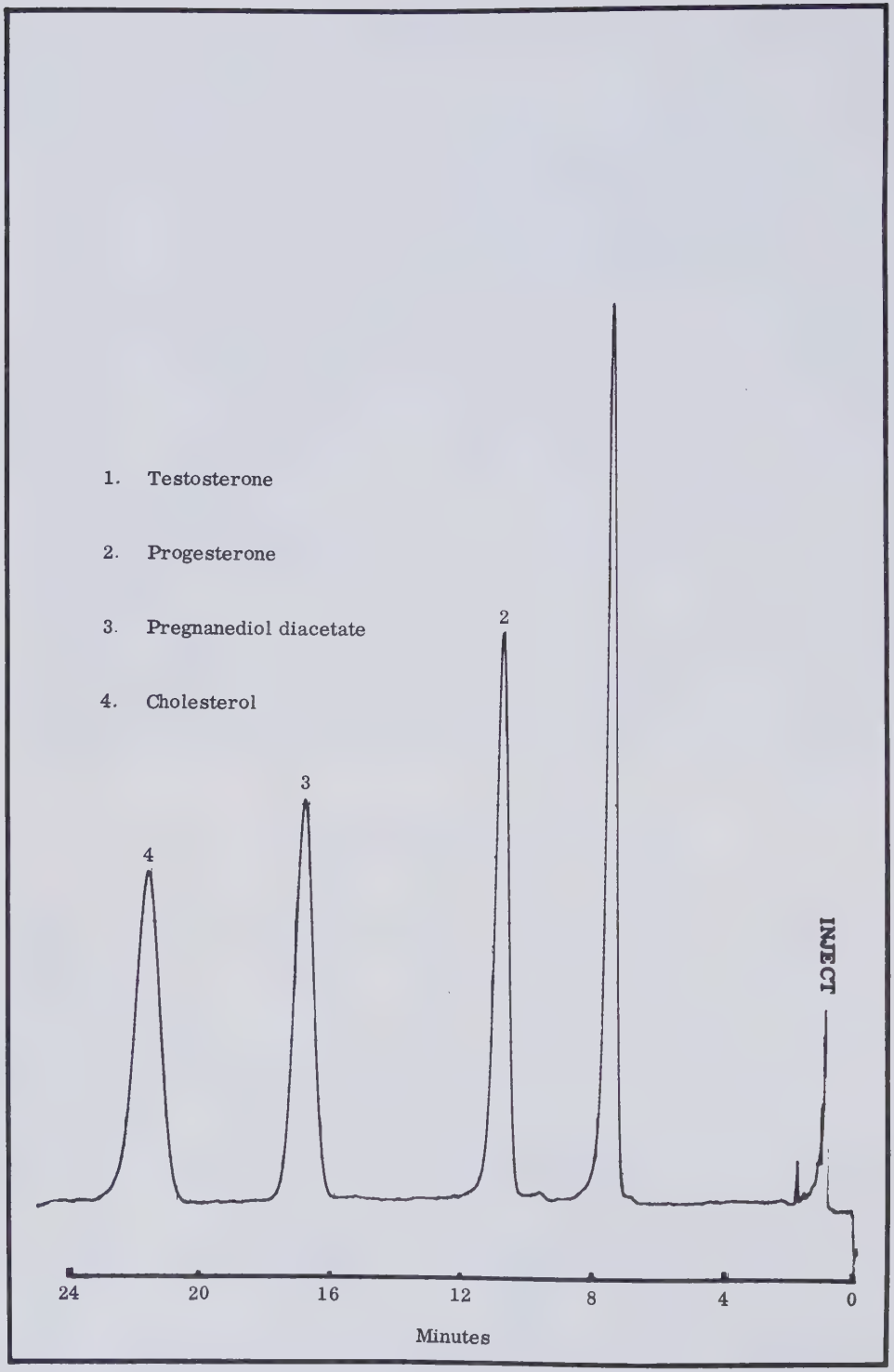
35b Part of the mass spectrum of a fungal derivative



36 A mass spectrometer tube arranged so as to show the effective parts



37 Graph showing separation of lower fatty acids by counter-current distribution



38 A gas chromatogram showing the separation of natural products, (in this case steroids)

Electrical methods of analysis

Electrogravimetric analysis -- in which an element is electrolysed quantitatively onto a suitable electrode and its amount determined by weighing -- really owes its inception to the demands of industry for a German metallurgical company offered a money prize for a rapid method of determining copper which would permit of some eighteen analyses in one working day. C. Luckow (1869) devised a suitable method and electrogravimetric procedures for zinc, cadmium, lead, manganese and mercury appeared in the next ten years. The most thorough basic studies were made by A. Classon (1843 - 1934) who wrote the first book on the subject, *Quantitative Analyses auf elektrolytischen Wege.* The cylindrical net and spiral wire electrodes used today were introduced by C. Winkler in 1899 and the idea of electrolysis at a fixed potential controlled by an auxiliary electrode was suggested and developed by H.J.S. Sand (1908).

Changes in the conductivity of a solution as a reagent is added form the basis of conductivity titrations first suggested by F.W. Kuster and M. Grüters in 1903. More recently (1946) J. Foreman and D.J. Crisp and, independently, F.W. Jensen and A.L. Parrack, modified the procedure and elaborated the technique of highfrequency titrimetry employing a.c. currents of frequencies 10^6 - 10^8 Hz: despite the greater complexity of the apparatus one advantage is that quite dilute solutions can be titrated and the electrodes can be placed outside the titration vessel, or even dispensed with altogether.

Polarography

One of the most significant applications of electrolysis is its use in polarography, a new technique first described in 1922 by Jaroslav Heyrovsky (1890 - 1967). The basic procedure is to allow drops of mercury to fall regularly, one in every 3-6 seconds, from a fine capillary (0.05 mm) through the solution that is to be analysed containing a 'supporting electrolyte' into a large pool of mercury which is made the anode with respect to the dropping mercury electrode. As the potential difference increases the cell current changes in a characteristic way and the 'limiting current' is proportional to the concentration of reducible material in the bulk of the solution. The 'half-wave potential' is characteristic of the ion being reduced though independent of its concentration.

In 1925 J. Heyrovsky and M. Shikata devised the first instrument in which, as the voltage across the polarographic cell was increased by a motor driven potentiometer, the polarogram was traced automatically on light sensitive paper: nowadays a pen recorder is used.

Determinations of reducible ions in the range 10^{-2} - 10^{-4} M could be carried out to $\pm 2\%$ and polarography was soon found to be of great importance in the metallurgical industry for determining traces of certain metals in ferrous and non-ferrous alloys. It is now used in many other fields for it serves for the determination of organic as well as inorganic compounds, for the continuous determination of oxygen dissolved in natural waters, and, by indirect procedures, even for elements such as thorium, zirconium, hafnium and tantalum whose ions are not reduced at the dropping mercury electrode.

Derivative polarography was suggested by Heyrovsky in 1947 as a means of estimating one component of a mixture in the presence of more easily reducible major constituents. This led to a number of instrumental improvements in the period 1948 - 1952 but the first real improvement in sensitivity followed studies in a.c. polarography in which a small alternating voltage is superimposed upon the slowly increasing direct current voltage. The improvement is even greater when a square wave form is used rather than a sinusoidal voltage (G.C. Barker and others, 1952) concentrations down to 10^{-8} M and less can now be determined with commercially available, albeit costly and complicated instruments. Pulse polarography (G.W. Barker and A.W. Gardner, 1958) is another development.

The rapid response of the cathode-ray oscillograph to the quickly changing potentials of the dropping mercury electrode was first exploited by Heyrovsky in 1941 and greatly improved by many subsequent workers, notably J.E.B. Randles (1948) and Barker (1958) using sophisticated electronic circuitry. The hanging mercury drop electrode (W. Kemula and Z. Kublick, 1957) and the rotating platinum microelectrode (H.A. Laitinen and I.M. Kolthoff, 1941) are only two of the many significant developments which have made polarography one of the most important modern techniques for use in aqueous and non-aqueous solutions and even in fused salts, and as the basis of other electrometric procedures.

Spectrography

As early as 1752 T. Melville had noted the yellow colour imparted to flames by sodium compounds and six years later A.S. Marggraf noted the lavender colour due to potassium. The crimson caused by strontium and the green produced by borates and copper compounds were observed by J.F.W. Herschel (1822) who also suggested the possibility of detecting traces of elements from their ability to colour flames. Although W.H. Fox Talbot (1834) described the use of a prism to resolve and distinguish between the red colours caused by strontium and lithium it was G. Kirchhoff (1824 - 1887) who in 1859 constructed the first with a wavelength scale. The fruitful collaboration of the physicist Kirchhoff with the chemist R.W. Bunsen (1811 - 1899), demonstrated that the spectrum of each element was different and characteristic and led in turn to the discovery of caesium and rubidium. Even more important was the discovery that the position of certain dark lines in the sun's spectra (discovered by J. Fraunhofer in 1814) coincided precisely with the bright lines emitted by flames containing sodium and other elements. If a bright light giving a continuous spectrum was passed through a yellow sodium flame the resulting spectrum showed a black line ('reversal spectra') in place of the familiar yellow line, from which they deduced that sodium must be present in the sun. In Bunsen's words "... this makes it possible for us to determine the composition of the sun and stars just as accurately as we can identify chloride or sulphate in the laboratory".

Although J.N. Lockyer (1836 - 1920) pioneered the introduction of photography into spectroscopy, quantitative spectrum analysis only developed during the present century; for it was soon realised that the number of spectral lines observable and their relative intensity depends on the method of excitation (by flame, arc, spark, etc) and also on the other elements present. Indeed, H. Kayser, the author of the comprehensive *Handbuch der Spektroscopie* concluded in 1910 that "quantitative spectrum analysis is impracticable". However, W. Gerlach's method of using "homologous line-pairs" (1925) using a suitable internal reference material proved to be the solution and the procedure was further refined by E. Schweitzer two years later and greatly simplified by the use of the logarithmic sector introduced by G. Scheibe and A. Neuhausser in 1928, for this substituted comparison of line lengths for the more difficult comparison of line blackening, as measures of relative concentration. Even so great care had to be taken in photographing spectra and in developing plates if strictly comparable results were to be obtained.

It must be stressed that the great advantage of the spectrographic method is that it is fast (and hence cheap in labour costs), reasonably sensitive under optimum conditions, and adaptable for the simultaneous determination of a large number of elements in the same sample: a minimum of chemical preparation is required, and sometimes none at all. A big step forward was made when H.G. Lundegårdh (1929) introduced photoelectric methods to measure the intensity of irradiation emitted at any chosen wavelength. If the dispersion is large enough, radiation from the internal standard, at a wavelength selected for each of various elements of interest, can be focused on a set of photomultipliers and and the intensities of the spectral lines compared electronically with that of the standard;

changes in the ratio correspond to changes in composition. The detailed composition of the sample can then be calculated and printed out as a series of percentages, and although this sophisticated instrument (e.g. the A.R.L. Quantometer or Hilger Polychromator) may be situated in a laboratory some distance away, a furnace operator can receive by teleprinter a detailed analysis of a molten alloy only a few minutes after taking the sample.

The number of lines found in a spectrum depends on the particular element and increases with the temperature to which it is heated. Lundegårdh pioneered high temperature flames (e.g. air-acetylene) into which a solution of the sample could be introduced as a fine spray. He can therefore be regarded as the founder of flame photometry (1928) although the possibility had been envisages by J. Janssen as long ago as 1870. By replacing the expensive monochromator by simple optical or interference filters with a photocell coupled to a simple potentiometer and direct reading galvanometer it has proved possible to devise relatively cheap instruments for the quantitative determination of e.g. sodium, potassium and calcium, determinations of importance to the clinical biochemist, the agricultural chemist and the manufacturer of fertilizers. Once again great care must be taken to keep conditions constant, i.e. the pressure of gases (often air and propane) and hence the temperature of the flame, the rate of aspiration, and the bulk composition of the sample solutions, if matrix (interelement) effects are to be minimised.

Atomic absorption spectroscopy

In a flame even as hot as 3000°C comparatively few of the atoms are excited and in a position to emit their characteristic radiation, for example with sodium about 6×10^{-2} % and for zinc about 6×10^{-8} %. In 1955 A. Walsh pointed out that it was possible to increase the sensitivity above that of emission spectroscopy by making use of all these unexcited atoms, since light of a wavelength corresponding to the emission radiation of an element is absorbed by its atomic vapour. The apparatus consists essentially of a hollow cathode lamp to produce the required atomic spectrum, an atomizer and spray chamber to conduct the sample into a long and narrow flame, and lenses to focus the transmitted radiation onto the entrance slit of a monochromator. The greater the concentration of the element aspirated into the flame the more the radiation from the hollow cathode lamp is absorbed and the less radiation passes through the monochromator onto the photomultiplier and its associated equipment, where the intensity is measured. This new technique can readily be used for over sixty elements in the range 0.1-10 parts per million. The accuracy is around $\pm 1\%$ in most cases, the technique is virtually specific, it is rapid and easy to operate with relatively unskilled staff. Inter-element effects are very much less than in emission spectroscopy, and interference can often be eliminated. Atomic absorption is extensively used for the determination of mercury and alkyl mercury compounds in fish and foodstuffs.

If the atoms generated in a flame (as in atomic absorption) are irradiated by resonance radiation from a powerful source fluorescence is generated and can be viewed at right angles to the incident beam. J.D. Winefordner and T.J. Vickers (1964) and T.S. West and his colleagues (1966) have shown that this newer technique of atomic absorption fluorescence may be several orders of magnitude more sensitive than atomic absorption spectroscopy and suitable for the analysis of 10^{-9} M solutions.

X-ray diffraction analysis

X-ray diffraction is a speedy method of examining powdered crystalline material and is extensively used in industry to examine and identify 'unknowns' - deposits, pigments, and samples of unknown provenance, before chemical analysis is resorted to. If a substance is irradiated by X-rays of very short wavelength a secondary emission takes place as C.G. Barkla and C.A. Sadler showed in 1907. However, it was not until 1945 that advances in instrumentation and electronics made it possible for H. Friedman and L.S. Birks (1948) to design an X-ray fluorescence spectrograph suitable for routine use. Each element gives a number of lines of different wavelength and relative intensity which can be used to identify it qualitatively. When no interelement interference occurs the graph of counts per second from the radiation counter versus the percentage of element present is a straight line, and so quantitative measurements are feasible too.

X-ray fluorescence is one of the most widely applicable techniques, although it cannot be used for elements of atomic number below 12 and the instrument costs some £20,000. It is very useful for determining halogens in organic compounds, traces of nickel, barium, zinc, lead, vanadium and sulphur in petroleum products, for various purposes in the plastics industries and even for the continuous monitoring of most heavy metals in process streams of finely divided minerals or ores.

Colorimetry

Although the natural colour of a substance or one produced by a suitable chemical reaction had been used in qualitative tests from the earliest times it was not until the nineteenth century that this property was used quantitatively although some correlation between concentration and depth of colour must have been obvious. The first use of colorimetry, or absorptiometry as it should more correctly be termed, occurred in 1838 when W.A. Lampadius estimated the iron or nickel content of a cobalt ore by matching the colour of its solution against that of solutions containing known concentrations of iron, cobalt or nickel, placed in cylindrical tubes. C. Heine (1845) determined the bromide content of mineral waters by adding chlorine water and a little ether and comparing the yellow to brown colour.of the bromide solution against that of a 'standard series' of ether extracts prepared similarly from 5, 10, 15 ..... 45 and 50 mg of potassium bromide. A. Jacquelain (1846) determined copper in terms of the blue colour formed on adding ammonia and T.J. Herapath (1852) determined iron as the red ferric thiocyanate complex.

The earliest instruments for matching the depth of colours by eye were those of A. Müller (1853) and F. Dehm (1864). In Jules Duboscq's colorimeter (1870) sample and standard solutions in adjacent glass cylinders with plane bottoms are uniformly illuminated from below: the transmitted light is reflected by prisms to form two contiguous semicircular patches on a glass plate viewed by an eyepiece. By a rack and pinion device the depth of each solution through which the light passed is changed until the colours match completely and only a single circular patch is seen.

For many purposes the 'standard series' of reference solutions can be replaced by a series of coloured glasses, and simple portable devices such as the Lovibond Comparator have been widely used for determining ammonia by the Nessler reaction, the pH of soil, the chloring content of swimming baths, and so on.

The relationship between the intensity, I_0, of incident light and that, I of the light emerging after passage through 1 cm of a solution of molar concentration c, which is nowadays expressed by the equation $\log (I_0/I) = \Sigma\ cl$ (where Σ is the molar absorption coefficient) can be attributed to the work of P. Bougouer (1729), F. Lambert (1760), F. Bernard (1829), A. Beer (1852) and R. Bunsen and H. Roscoe (1857). Its importance lies in demonstrating the linear relationship between the concentration and the term $\log (I_0/I)$ called the absorbance or (formerly) optical density. C. Vierordt devised the first instrument in which the intensity of a beam of light could be reduced by an adjustable, calibrated slit until it matched that leaving the sample solution. He used it to determine permanganate, chromate, copper, fuchsin and blood stains. In 1877 P. Glan and C.G. Hüfner independently devised instruments in which the optical attenuation was produced by polarizing one or both of the light beams, a technique now almost obsolete.

Spectrophotometry

A spectrophotometer employing a barrier-layer photocell to replace the human eye was first constructed by Berg in 1911 and successive improvements led to a commercially available instrument employing two photocells in opposition with a sensitive galvanometer. The light traversing a rectangular cell containing solvent only (the 'blank') was attenuated by an adjustable diaphragm calibrated logarithmically until it matched the intensity of light passing through the sample and the galvanometer gave a null reading. Sensitivity was improved by using a set of glass filters to restrict the light to a narrow band of wavelengths and a mercury vapour lamp could be used to give an intense line source for certain special determinations. Such instruments played a most significant role in introducing a whole range of rapid absorptiometric procedures into metallurgical and other laboratories.

Based on extensive academic research and the need for even more precise and versatile instruments covering both visible and ultraviolet ranges, the Beckman Instrument Company of America produced a spectrophotometer around 1945 which set the standard for some years. It incorporated a monochromator with a quartz prism and optics, adjustable slits, a tungsten-filament lamp for the visible region and a hydrogen-discharge lamp for measurements from 360-210 nm with red and blue-sensitive phototubes for the appropriate regions. Photocurrents from sample and blank solutions were amplified electronically and the absorbances in the range 0-2.0 could be read off on a dial at any wavelength in the range 200-1000 nm. Cell lengths of 2-100 mm could be accommodated in a thermostatted cell compartment. The Unicam S.P.500 spectrophotometer manufactured in this country offered the same facilities and introduced precision spectrophotometry in the ultraviolet and visible regions at a cost of the order of £1000. A multiplicity of spectrophotometers is now manufactured in many different countries and to different specifications.

Contemporary advances in electronics and instrumentation and the increasing demands of technology have brought the practice of absorptiometry and the ancillary technique of spectrophotometric titrations within the reach of every laboratory and have in their turn stimulated a constant flow of new procedures for determining inorganic, organic and biological material of all sorts. Spectrophotometers with 'flow-through' cells are available for the continuous monitoring of absorbing liquids. Fully automatic recording instruments represent one obvious way in which designs have proceeded; the need to process a large number of samples in succession has given rise to instruments which will automatically read the absorbance of a sample at a number of predetermined wavelengths in succession, print out the answers, and then replace the sample by the next one. This then provides data needed for computing the concentrations of several components present in each sample.

Whereas absorption spectra in the ultra-violet or visible regions arise from electronic excitation on the absorption of suitable radiation, the vibration of constituent atoms in a molecule gives rise to infra-red, spectra and the rotation of the whole molecule to far infra-red, and microwave spectra. In the longer wavelength region involved in infra-red work

(1-100 microns) a diffraction grating must be used in place of a prism and lenses must be replaced by mirrors; optical cells have to be made of rock salt, calcium fluoride or potassium bromide. The light source must be replaced by a source of steady heat, and the photocell by a bolometer or a heat detecting cell such as that devised by M.J.E. Golay in 1947. Problems of amplifying the small electrical signals and minimising the noise to signal ratio and ensuring stable operation become severe.

Although by 1928 J. Lecompte had already listed many absorption bands characteristic of particular atomic groups and E.D. McAlister (1936) had described an accurate method for determining carbon dioxide in the air, progress was slow - though pioneer work by J.J. Fox and A.E. Martin in the Government Laboratory (1940 - 1947) revealed the analytical possibilities for identifying the components of complex mixtures. It was shown, for example, that phenol from coal tar always contained naphthalene, from benzenesulphonic acid ortho- and para-hydroxydiphenyls, and from chlorobenzene small amounts of diphenylether.

The demand for high octane petrol for aeroplanes during the Second World War (1939-1945) created a number of new analytical problems, and wartime research by H.W. Thompson and G.B.B.M. Sutherland in England did much to improve knowledge and design equipment in this new field. However, it was certainly in America that infra-red analysis made the greatest strides. The American Cyanamide Co., probably constructed the first instrument in 1936 and could state by 1943 "Daily this tool is performing analyses impossible by other methods: more common analyses are being completed in minutes which previously required hours". Improvements in amplifying the small a.c. voltages obtained from infra-red detectors by 'chopping' (McAlister, 1936), the introduction of the first double-beam instrument (N. Wright and L.W. Herschel, 1947) the first double-beam prism-cum-grating instrument (A.E. Martin, 1955) are a few landmarks in a field dominated by the work of commercial firms and large organisations, where improvements in instrumentation have followed one another so rapidly that commercial apparatus, now quite freely available, becomes out of date, like motor cars, inaa matter of years.

The ability to scan and record a complete spectrum from 3-30μ in a few minutes, or to examine part of this at greater amplification is particularly important since no great skill is required and individual spectra are so rich in bands and are altered characteristically by even small changes in the composition of the sample that they serve almost as fingerprints for the purposes of qualitative identification: to this end elaborate card-index systems of recorded spectra are available. Apart from complete identification much information can be gleaned about the composition of an organic material since each arrangement of atoms, for example C=O, -CO.O-, -NH_2, -CH=CH-, -C≡C- etc., gives rise to characteristic bands whose relative intensity and position vary little from compound to compound and have been carefully listed in tables of group and band frequencies.

In addition to detecting the presence and nature of impurities in a sample, quantitative analysis is equally possible. Gases are examined in long cells, solids after grinding up finely with 'Nujol' or by compression with powered potassium bromide into a glass-like disc: liquids are contained in verytthin cells. It would be difficult to find areas in inorganic, organic and industrial chemistry where infra-red analysis is not used to advantage.

Mass spectrometry

Spectra of quite another sort, the mass spectra due to positive ions were first studied by W. Wien (1898) and J.J. Thomson (1911) who showed that different elements could be distinguished by their different mass-to-charge ratios. A.J. Dempster (1918) and F.W. Aston (1919) made significant advances in resolving and recording mass spectra. In a typical advanced modern instrument a resolving power of 25,000 is possible and although the ions CO^+, N_2^+, CH_2N^+, and $C_2H_4^+$ all have the same nominal mass of 28, they can be distinguished by their actual masses measured accurately as 27.994914, 28.006147, 28.018723 and 28.031299 respectively. Indeed the mass spectrograph now plays a very significant role in the precise analysis of organic compounds since each line in the mass spectrum corresponding to a particular ion is always accompanied by others due to the heavier isotopes ^2H (deuterium), ^{13}C, ^{15}N, ^{17}O and ^{18}O, and of varying heights dependent on their relative abundance. For example, a line of mass 422 in the spectrum of a natural product of accurately determined mass 422.223 ± 0.004 was found to be accompanied by isotopic lines at 423 and 424 of relative heights 32.62 and 6.05%. By reference to J.H. Beynon and A.E. Williams' *Mass and Abundance Tables for use in Mass Spectrometry* (1963) we find that such a combination could only originate from a compound of molecular formula $C_{30}H_{30}O_2$, and further information on its structure can be inferred from the masses of the ions produced by fragmentation and recorded simultaneously -- all from a few milligrams of sample.

O. Eisenhut and R. Conrad (1930) appear to have been the first to investigate the behaviour of hydrocarbons in a discharge tube and only ten years later H. Hoover and H.W. Washburn, using a commercial version of Dempster's mass spectrograph were able to determine quantitatively the constituents of a complex hydrocarbon mixture. Progress became so rapid that by 1947 mass spectrometers in petroleum refineries had replaced the lengthy and tedious technique of low-temperature distillation and were used for continuous analyses for process control. As many as 40 components can be determined simultaneously in a mixture by linking the output of a mass spectrometer to a computer.

The analytical applications of the mass spectrograph are legion. It can be used to determine as little as 10^{-8} g of hydrogen or 10^{-7} g of oxygen or nitrogen in gases evolved on melting metals in vacuo, for determining 40 or more elements at the same time in semiconductors at levels below 0.01 p.p.m. for the determination of traces of neutron absorbing elements such as boron or the rare earths in graphite for nuclear reactors, for a host of difficult and time consuming analyses in metallurgy, and as an adjunct to the gas chromatograph for identifying the complex mixtures responsible for the aroma of coffee, the flavour of foodstuffs, or the material responsible for unpleasant 'taints' in battery chickens.

The ability to distinguish between isotopes of the same element and to measure their relative abundance is especially valuable in isotope dilution analysis. For example when 1.8μ g of enriched lithium with $^7Li/^6Li = 0.004$ was intimately mixed with 127 mg of graphite containing normal lithium ($^7Li/^6Li = 12.4$) the isotopic ratio was found to change to 1.13, showing that the graphite contained 21.1 p.p.m. of lithium. This sensitive method

is completely specific and since the result depends only on an abundance *ratio,* quantitative separation of the element concerned is unnecessary. Mass spectrographs are particularly valuable for determining the age of rocks or mineral specimens by measuring abundance ratios in the uranium-lead-thorium, the rubidium-strontium, and the potassium-argon methods.

Radiochemical analysis

Radioactivity is an atomic property: for in certain isotopes the nucleus is unstable and disintegrates spontaneously to give daughter elements while emitting characteristic radiation in the form of α, β or γ rays, and decaying with a characteristic 'half-life' which is independent of the temperature, the amount of element, its physical state or the way in which it is chemically combined. Analytical applications of radiochemistry only became common when convenient means of measuring radioactivity became available, and the history of the development of such instruments as the Geiger-Müller counter (1908-1928), the scintillation counter (1908-1947), the proportional counter, and associated equipment such as scalers and rate-meters cannot be given here. Progress was especially rapid during and since the second World War and it would not be wrong to assert that the scope and procedures of present-day radiometric techniques have been strongly influenced by progress in electronics and instrument manufacture. For example, a γ -ray spectrometer will now accept and record up to 100 different energy levels. A second γ -ray spectrum taken 1 minute, 10 minutes, 2 hours, etc., later will give information about rates of decay and hence identify the elements present and, by comparison with standards, their amount.

G. von Hevesy and F. Paneth (1913) were really the first to show how radioactive isotopes could be employed as tracers to determine the solubility of lead sulphate. By 'labelling' with radioactive ^{198}Au, O. Erbacher and K.Z. Philipp (1935) were able to follow the chemical separation of gold and platinum. R. Ehrenberg (1925) pioneered the use of radioactively labelled reagents using, e.g. a radioactive lead salt to precipitate chromate which he was then able to determine from the activity of the lead in the precipitate. Radiometric titrations were first attempted by A. Langer (1941).

Initially, such applications of radiotracers were limited to the few naturally occurring isotopes readily available and of convenient half-life and activity. With the advent of the large scale nuclear reactor, radioactive isotopes can be obtained for almost all elements, and the device of labelling is regularly used to examine the efficiency of separations by precipitation, volatilisation or liquid-liquid extraction, to measure losses by absorption and, in short, to check and supplement all the procedures of classical and physical methods of analysis. It has many applications in industry, e.g. to study frictional wear in bearings, to see how long materials remain in mixers of fluid-bed processes, how efficient stirrers are: for although this method of obtaining information is not strictly analytical, it does replace analyses which might be very expensive and difficult to carry out. Labelled organic compounds are invaluable in biochemistry for studying the flow of blood *in vivo* or for elucidating the complexities of biochemical syntheses or metabolic pathways.

Isotope dilution analysis, described above in connection with mass spectrometry, can be used even more easily and widely with radioisotopes. For example the difficult determination of γ -benzenehexachloride in insecticides can be carried out using γ -$C_6H_6C1_6$ labelled with ^{36}Cl.

In 1936 von Hevesy and H. Levi were the first to carry out an entirely new kind of analysis, one which has since achieved very great importance. By bombarding with neutrons

from a radium-beryllium source they were able to show that a sample of the yttrium contained less than 0.1% of the rare-earth dysprosium. The basic procedure of the modern technique of neutron activation analysis is to expose a known weight of sample containing the element that is to be determined together with a standard containing a known and similar weight of this element to an intense flux of neutrons. After removal from the source of radiation a known weight of inactive element is added to each as a 'carrier' and a specimen of some completely pure compound of the desired element is separated from all the other elements present, weighed, and counted. From the weight of added carrier it is easy to calculate what the activity would have been had there been no losses in the chemical processing; the weight of element in the sample then follows from that of the standard and their relative specific activities.

Since no more radioactive isotope is produced from the moment the irradiated sample and standard are removed from the neutron source, no errors are introduced if the reagents used in the subsequent chemical processing contain any of the element being determined: there are thus no problems due to 'blanks'. The procedure is absolutely specific and the sensitivity is often very high indeed. For example, with a flux of 10^{12} neutrons/cm^2/sec (100 times smaller than that of many commercial reactors) it is possible to determine 10^{-12} g of e.g. dysprosium, europium, gold, holmium and lutecium, and less than 10^{-8} g of some 70 other elements. Apart from such important applications as the determination of traces (less than 10^{-10} g) of arsenic in germanium required for the manufacture of semiconductors, it has been used in forensic investigations to analyse the amount of arsenic in different parts of a single hair from a murdered woman. The fatal dose produced a high concentration of arsenic at the root, and as the rate of growth of the hair is known, the approximate dates on which previous, non-lethal doses had been administered could be calculated with some confidence.

The analysis of complex mixtures

The most persistent feature of analysis during the last 50 years has been the increasing need to determine smaller and smaller amounts of substances in complex mixtures, often available themselves only in small amount. Some of these problems have arisen through increasing activity in biochemistry ("what amino-acids are present in this small sample of hydrolysed protein - and how much of each?"), some from the increasing complexity of industrial problems ("what materials are present in this catalyst or sample of plastic from a rival manufacturer?"), many from the current concern with environmental pollution ("how much lead is there per cubic foot of air taken from the city centre?" or "What detergent is present in this river or lake -- and how much of it?"). From microscopic fragments of glass or paint found after an accident or at the scene of a crime the police may seek to identify the make of car involved and even its year of manufacture. Many widely applicable procedures for separating complex mixtures are now available and some of these are specially suitable for pre-concentrating the components of a sample to bring them within the accessible range of reliable methods for their ultimate determination.

The oldest of these procedures is solvent extraction, long familiar in various technological processes connected with the preparation of perfumes and drugs. The earliest application in inorganic chemistry appears to be the use of ether by E. Péligot (1842) to extract uranium salts from aqueous nitric acid, a procedure revived in the early days of the atomic energy industry. W. Skey (1867) proposed the separation of various metal thiocyanates by liquid-liquid extraction but there is no record of his actually performing the experiments. J.W. Rothe (1892) introduced the important ether extraction of iron (III) from its solution in concentrated hydrochloric acid and much later E.H. Swift (1924) extended the technique to gallium. R. Bock and his co-workers made a detailed survey of the extraction of a very wide variety of chlorides, thiocyanates (1942, 1951), nitrates (1950), bromides (1953) and even fluorides (1956).

The first account of the extraction of a formally uncharged metal chelate was given by P. Cazeneuve (1900) who extracted chromium (III) into benzene containing 1,5-diphenylcarbazide, and the same reagent was used by F. Feigl and F.L. Lederer (1925) to effect certain separations. However, the most significant date for analytical chemistry was 1925 when Helmuth Fischer introduced the coloured organic compound dithizone, $C_6H_5.NH.NH.CS.N{=}NC_6H_5$. Although this has been prepared in 1898 by Emil Fischer who had noted the formation of a red, insoluble lead salt, it was Helmuth Fischer who showed that the green reagent formed deeply coloured red, orange, yellow or violet complexes with a limited number of metals, that these were insoluble in water but could be extracted into water-immiscible solvents such as chloroform, carbon tetrachloride or benzene. The reactions could be made highly selective by controlling the pH of extraction and the use of 'masking' reagents. He also designed many new absorptiometric procedures suitable for determining microgram quantities of metals such as silver, mercury, copper, zinc, cadmium, lead, bismuth and thallium. Since then over 2500 papers have been published dealing with the uses of this reagent alone and extensive studies have been made of other com-

plex-forming reagents among which thenoyltrifluoroacetone is especially noteworthy since it was specially designed by J.C. Reid and M. Calvin (1959) to facilitate the extraction of transuranium elements and to handle separations encountered in wartime atomic energy projects.

In 1949 J.C. Warf introduced in tributylphosphate, the first of a large number of organic phosphorus compounds that have since played an increasing role in liquid-liquid extraction. The separation of rhenium from molybdenum by extracting tetraphenylarsonium perrhenate into chloroform (S. Tribalat, 1951) be seen as the precursor of many procedures involving the extraction of ion-pairs and the currently increasing uses of long-chain amines and sulphonic acids as 'liquid ion-exchangers'. The synergic effect produced by the simultaneous use of two extracting agents (H. Irving and D.C. Edgington, 1961) has also proved important.

An important concept in liquid-liquid (or other) separation processes is that of the distribution coefficient, K_A, defined here simply as the ratio of the analytically determined concentration of the species A in the organic phase to the analytically determined concentration in the aqueous phase with which it is in equilibrium. If an aqueous sample contains two substances, A and B, such that K_A is greater than K_B the result of a single extraction will be to increase the proportion of A in the organic phase and to reduce it in the aqueous phase. If the aqueous phase is again equilibrated with fresh solvent the proportion of B to A will be further increased. By a succession of such 'batch' extractions a sample of A can be obtained as free from B as desired, and conversely. If the original sample contains a number of components each with a different distribution coefficient then, by using a large number of equilibration stages (e.g. separating funnels) and a large number of systematically planned operations ('transfers') the various components will tend to separate as illustrated below. Under optimum conditions some components can be obtained virtually pure, but at the expense of a diminished yield.

Apparatus for such multiple distributions by the 'counter-current' principle has been devised by many scientists, especially for use in biochemical separations and a wide variety of 'mixer-settler' units have been devised with the needs of the atomic energy and other industries in mind.

Chromatography

The separation procedures now classified under the general title of chromatography are also counter-current processes involving the distribution of material between two phases. However, it is not a batch but a column process and bears the same relationship to a single separation stage as distillation with an efficient fractionating column does to a simple distillation. Since the various possible combinations of liquid-liquid, liquid-solid, gas-liquid, and gas-solid chromatography were intensively developed over much the same period, in what has been some of the most prolific and fruitful years in the history of analytical chemistry, the following account is necessarily incomplete in view of the space available.

Pliny (23-79) in his *Naturalis Historia* described a test for dyes by spotting their solutions onto papyrus. Traditional practice in the dyeing industry was likewise to apply drops to absorbent paper and note the pattern of concentric coloured rings due to the various constituents, a process refined by F.F. Runge (1795-1867) whose rare book *Der Bildungstrieb der Stoffe* (1855) was illustrated by coloured circular chromatograms stuck in by hand. Following on some early work by C.F. Schönbein (1861), E. Pischer and E. Schmidmer (1892) demonstrated the separation of sodium and barium chlorides and of ammonium and ferrous ions on filter paper. The technique was fully investigated by Schönbein's pupil F. Goppelsroeder whose book *Kapillaranalyse* gave the name to the procedures which have been extensively developed in recent years for group separations, (F.H. Burstall, G.R. Davies, R.P. Linstead and R.A. Wells, 1950), M. Leder (1949-50), F.H. Pollard and J.F.W. McOmie (1949-) and others on both large and small scales, leading in many cases to quantitative determinations of traces of certain cations in admixtures. Separated spots (or rings) due to various cations can sometimes be detected by their own colour but are more usually 'developed' by spraying with a suitable colour-developing reagent. The use of the R_f value (the ratio of the distance moved by the substance to that of the solvent front), a term introduced by A.J.P. Martin and R.L.M. Synge in 1941, can be used to identify the components of chromatograms run under strictly reproducible conditions. G.M. Schwab and K. Jockers (1937) and H. Flood (1940) used columns of alumina or paper impregnated with alumina to separate mixtures of cations.

The use of columns of alumina to separate organic materials -- absorption chromatography -- is usually attributed to the botanist Mikhail Tswett (1872-1919) although Reed (1893) was the first to use columns packed with powdered absorbents and D.T. Day noted the separation of different fractions of crude petroleum on passage down a column of powdered limestone (1897). Tswett's classical experiment (1906) was to add an extract of green leaves in petroleum ether to the top of a column of finely powdered calcium carbonate and to elute with pure solvent. A slow moving, pale yellow band, two green and three yellow bands gradually developed along the column, demonstrating the composite nature of chlorophyll. The xanthophylls, carotenes and chlorophyll-a and chlorophyll-b were separated and subsequently identified and it is noteworthy that the last two possessed very large molecules that differed only in having $-CH_3$ replaced by -CHO. The name

chromatography, applied to such procedures has been retained even when the substances involved are colourless.

After being forgotten for 39 years R. Kuhn, A. Winterstein and E. Lederer revived this procedure in their separations of carotenoids (1931) and absorption chromatography rapidly became a widely established technique, especially in organic chemistry and biochemistry.

A most important new application of liquid-liquid extraction began in 1941 when A.J. P. Martin and R.L.M. Synge transformed it into a column chromatographic procedure by the elegant device of holding one phase stationary on a porous support (e.g. water on silica gel) and using as the mobile phase a solvent immiscible or only slightly miscible with the stationary phase. If two solutes have different distribution coefficients the one more soluble in the mobile phase will travel faster and emerge first as more solvent is added to the top of the column. In this general procedure of partition chromatography various methods have been devised for improving the separation of successive components e.g. frontal and elution analysis, (S. Claesson, 1946), displacement analysis (A. Tiselius, 1940, 1950) and gradient elution analysis (R. Alm and R.J.P. Williams, 1951). Reversed phase chromatography in which the organic solvent becomes the stationary phase and an aqueous solution the mobile phase was developed shortly afterwards.

In 1944 R. Consden, A.H. Gorden and A.J.P. Martin used strips of filter-paper as the insert support for the stationary water phase. If the solution to be analysed (e.g. of mixed amino-acids) is applied to the top left-hand corner of a square strip of such paper and dipped in a trough of (say) phenol in an atmosphere of ammonia and coal gas, an ordinary 1-dimensional chromatogram results. If the paper is removed, dried, turned through 90 degrees and dipped in a trough of a different reagent (say) collidine containing a trace of diethylamine, each band of the original chromatogram will form the starting sample for a further chromatographic separation and a more highly resolved 2-dimensional chromatogram will result.

The separation of gases or organic vapours on a solid support with an inert gas as a moving phase was also suggested by Martin and Synge (1941) and studied by N.C. Turner (1943) for the separation of gaseous hydrocarbons. S Claesson (1946) made the first thorough study of separations on active charcoal and his procedure was simplified and improved by C.G. Phillips (1949). A really significant new departure was the first account of gas-liquid chromatography by A.J.P. Martin and A.T. James (1952) who separated all the fatty acids up to C_{12} by means of a heated column of silicone oil absorbed on 'Celite' with nitrogen as the carrier gas. The importance of this technique cannot be overemphasised for it lends itself to the separation of all materials that can be passed through a heated column as vapours without suffering decomposition: literally hundreds of papers dealing with applications of this technique appear annually, for even metals can be chromatographed as their volatile metal chelates and non-metals as their volatile alkyl or aryl derivatives.

Gas chromatography is used daily for determining the alcohol content of blood samples, for the routine examination of petroleum feedstocks and for many volatile commercial intermediates. It has advantages over even the mass-spectrometer when dealing with complex mixtures since it does not require elaborate computational aids in working out the results. However, the combination of gas chromatography followed by a mass-spectrometer to examine each fraction as it emerges is unrivalled in the field of flavour analysis.

Apart from constant improvements in the composition of the stationary phase designed to promote greater selectivity and better separations, much of the modern development is on the instrumental side and especially noteworthy are the devices for detecting minute

amounts of species emerging from the column. Katharometers, density balances, and latterly flame ionisation detectors, have been devised which produce electrical signals suitable for amplification and recording.

Thin layer chromatography (t.l.c.), the most recent chromatographic technique really dates from the work of N.A. Ismailof and M.S. Schraiber (1938) and the use of 'chromatostrips' for separating various terpene derivatives. (J.M. Miller and J.G. Kirchner, 1953). The modern development (E. Stahl, 1956) employs a very thin layer of absorbent on a glass plate as the stationary phase, and development of the chromatogram proceeds as the mobile phase percolates through it. Separations may be effected by absorption, partition, exclusion or ion-exchange, and t.l.c. may be regarded as a development of column chromatography which owes its present widespread use to its convenience and simplicity, the sharpness and speed of separations and the ease of recovering the separated constituents of a mixture.

When charged particles in solutions are subjected to an electrical field of say 10-100 volts per cm they migrate at rates depending upon their charge, size, and shape. If this separation technique of electrophoresis is carried out in gels there is an additional sieving action which provides extremely high resolving power. For example, since each species of fish contains a number of different proteins which can be separated by electrophoresis in a polyacrylamide gel to form a distinctive pattern of bands, this technique enables the analyst to identify even a tiny portion of fish and indeed to determine the origin of a 'fish finger'.

Ion-exchangers have been known for over a century for J.T. Way and H.S. Thompson (1850) described how ordinary soils could remove ammonium ions from solutions. In 1905 R. Gans synthesised base exchange materials which he called 'permutits' which were extensively used in industrial and domestic water-softeners.

B.A. Adams and E.L. Holmes (1935) described the preparation of synthetic resins for cation and anion exchange and a tremendous variety are now produced throughout the world. An ion exchanger can be defined as a solid insoluble in water and which contains a cationic (or anionic) species that is reversibly exchangeable with a different cationic (or anionic) species supplied from an external solution. Ions differ in the way they distribute themselves between the solution and the resin phase and once again separations are possible. The separation of individual rare earths from a mixture containing all of them (or the comparable separation of actinides) is an extreme example of their enormous potential in analytical chemistry.

Only a brief mention can be made of a modern version of liquid partition chromatography which can now compete more favourably with the speed and versatility of gas chromatography since uniform microspheres are used as the solid packing in a narrow column of hard-glass or steel down which liquids are forced at high pressure (J.J. Kirkland, 1971). Molecular sieves, solids with regular sizes pores of molecular dimensions ranging from 3.8 to 15Å are in current use for they have very selective absorption and exclusion properties that lend themselves to chromatographic separations.

Nuclear magnetic resonance

A very recent analytical technique is that of nuclear magnetic resonance (NMR) in which a sample containing a magnetic nucleus (such as ^{1}H, ^{11}B, ^{13}C, ^{19}F, ^{31}P and many others) is placed in an intense and uniform magnetic field and subjected at the same time to a radiofrequency alternating field. Absorption of energy gives rise to spectra corresponding to transition of nuclei among various permitted orientations. First observed in bulk matter by E.M. Purcell, H.C. Torrey and R.V. Pound and independently by F. Bloch, W.W. Hansen and M. Packard in 1945, the technique developed rapidly as soon as the commercial instruments, despite their great cost, became available.

The position of a band due to any particular atom relative to that of an internal standard, depends on the nature of the chemical molecule it is contained in: this 'chemical shift' is valuable diagnostically as is the splitting of a band into a doublet, triplet . . etc. due to spin-spin interactions with nearby nuclei. In any compound, organic or inorganic the total intensity of a peak is proportional to the number of equivalent magnetic nuclei present and in ethanol, for example, the areas of peaks due to -OH, $-CH_2$, and $-CH_3$ in the proton magnetic spectrum are in the ratio 1 : 2 : 3. Such 'proton counting' and 'total hydrogen analysis' are among useful features, for the technique is non-destructive and all the sample can be recovered unchanged. NMR is useful for determining the water content of many agricultural and food products and new uses are constantly being developed.

It will be easy to find techniques such as distillation, electron spin resonance, many varieties of thermal analysis, and so on which have escaped mention. Analytical chemistry has certainly come a long way since the technology of the early civilizations began to create demands for a variety of methods of testing. It might seem that with the formidable armoury of techniques and instruments mentioned above there would be no difficulty in answering any questions of the form "What's in it -- and how much?". Yet as the problems grow in number and complexity so must the skill and adaptability of the analytical chemist; for this is a permanent battle in which there can be no ultimate victory, despite the many triumphs along the way.

Suggestions for further reading

The most comprehensive and fully documented book is *History of analytical chemistry* by F. Szabadvary (1966). It is thin on techniques developed in the period 1920 - 1940 and many procedures developed since that time are not mentioned at all. Nevertheless it is still an essential work.

Some accessible and well-illustrated articles on particular subjects:
(Principles of chromatography) A J P Martin, *Endeavour,* 1974, **6,** 21 - 28
(Analysis of inorganic compounds by paper chromatography) F H Pollard and J F W McOmie, *Endeavour,* 1961, **10,** 213 - 221
(Some recent advances in chromatography) Arne Tiselius, *Endeavour,* 1952, **11,** 5 - 16
(Gas - liquid chromatography) A T James, *Endeavour,* 1956, **15,** 73 - 78
(X-ray fluorescence in chemical analysis) E T Hall, *Endeavour,* 1959, **18,** 83 - 87
(Polarography) G C Barker and G W C Milner, *Endeavour,* 1961, **20,** 26 - 31
(Volumetric analysis) F Greenaway, *Endeavour,* 1962, **21,** 91 - 97
(Mass spectrometry in organic chemistry) J H Beynon, *Endeavour,* 1966, **25,** 79 - 83
(Atomic analysis in flames) T S West, *Endeavour,* 1967, **26,** 44 - 49
(Centenary of Penny's process) H Irving, *Science Progress,* 1951, **153,** A 63 - 6

There are numerous articles in the *Journal of Chemical Education and Chemistry* in Britain, which serve as introductions to modern techniques and which often contain historical material.

The best paper-back to convey a feel for the whole field of analytical chemistry is H N Wilson's *An approach to chemical analysis* (1966). It combines a historical and philosophical approach with the appreciation of economic, human and practical considerations expected from the distinguished head of an analytical division of a very large industrial concern.

Another paper-back, *Analysis in the chemical industry* by L A Haddock (1968) is written from a different viewpoint and is illustrated with many photographs of contemporary equipment.

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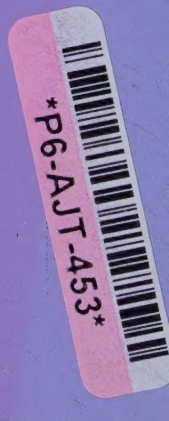

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